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CONTENTS

PAGE

The Chest Lead Electrocardiogram in Health. By AUDREY LEATHAM 215

The Early Diagnosis of Phaeochromocytoma. By LESLIE COLE 232

Cyclopropane Anæsthesia and Ventricular Arrhythmias. By MICHAEL JOHNSTONE 239

Angina Pectoris and Thyrotoxicosis. By WALTER SOMERVILLE AND S. A. LEVINE 245

Cardiac Anomalies in Mongolism. By PHILIP RAINSFORD EVANS 258

Embolism in Mitral Stenosis. By GEOFFREY BOURNE 263

Ventricular Septal Defect in Early Childhood. By R. M. MARQUIS 265

Atrial Septal Defect. By I. M. BARBER, O. MACGIBBON, AND PAUL WOOD 277

Angiocardiography in Heart Disease in Children. By RODOLFO O. KREUTZER, JUAN A. CAPPELLI, AND FREDERICK M. WESSELS 293

Primary Pulmonary Hypertension. By W. D. BRINTON 305

Abstracts 318

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THE CHEST LEAD ELECTROCARDIOGRAM IN HEALTH

BY

AUBREY LEATHAM

From the Cardiac Department of the London Hospital

Received August 19, 1949

The purpose of this paper is to describe the normal pattern and variation of the electrocardiogram in the chest leads in common use. Standards for the limb lead electrocardiogram in health have been determined by many investigators including Lewis and Gilder (1912), Jensen, Smith, and Cartwright (1932), Shipley and Hallaran (1936), Ashman and Hull (1937), Chamberlain and Hay (1939), Barnes (1940), Hoskin and Jonescu (1940), Pardee (1941), Hall, Stewart, and Manning (1942), Graybiel and others (1944), and Stewart and Manning (1944). In the same way, the normal appearance of certain chest lead electrocardiograms have been described by Kossman and Johnston (1935), Sorsky and Wood (1937), Wood and Selzer (1939), Deeds and Barnes (1940), Shanno (1940), Larsen and Skúlason (1941), Myers and others (1947), Grewin (1948), and Dolgin, Grau, and Katz (1949). Comparisons have been made by some of these authors and by others, including Groedel (1939), Wolferth and Wood (1940), Hecht (1942), Wallace and Grossman (1946), and Hull, Tucker and Weilbaecher (1948).

In this investigation 100 healthy adults were personally examined clinically, radiologically, and electrocardiographically. The leads in each subject included standard limb leads and unipolar limb leads (not analysed in this paper), and chest leads in positions 1 to 6 (American Heart Association, 1938) and in position 7 in the posterior axillary line (Evans and Hunter, 1943); the indifferent electrode was connected to the right arm (CR), left leg (CF), and through resistances to Wilson's central terminal (V), while the exploring chest electrode (Burger's suction type) remained in the same position. Standardization was normal (1 mv.=1 cm. deflection) or half normal (1 mv.= 0·5 cm.). The unipolar limb leads were taken by Wilson's method using resistances with standardization to one and a half times normal (1 mv.=1·5 cm. deflection), or normal, or twice normal in some of the earlier records. The entire technique was carried out by the author to eliminate personal variation.

The CR and V leads were taken in all subjects, but the CF leads were discontinued after the first 50 (aged 40 to 71 years) because of their variability. The voltage at the chest electrode was usually much higher than at the indifferent electrode, whether CR, V, or even CF was used, so that the pattern of the chest lead electrocardiogram depended more on the position of the chest electrode than on the choice of the indifferent electrode (Wilson, 1937). When the findings were common to CR, V, and CF, the chest leads were referred to as C1 or C2 or C3, etc.

Of the 100 healthy adults the majority were males; 50 were between the ages of 18 and 40 years (average 27), and 50 were between 40 and 71 years (average 53). They were without symptoms or abnormal physical signs and the blood pressure was always normal. Fluoroscopy of the heart and chest was normal. The records were always taken on a couch in the semi-recumbent position. The majority of the younger subjects were either medical students, medical officers, or hospital porters. Many of the older group had indigestion, but the pain of coronary artery disease was not simulated; if there was doubt they were excluded. It happened that the subjects were seldom stout, but six women with cyesis were deliberately included.

All records were taken with the Elmqvist three-channel electrocardiograph which had a frequency response about linear to 400 cycles, and consisted of valve amplifiers with resistance capacity coupling and oil damped mirror galvanometers. The results for the P, Q, R, S, S–T segment deviation, and T waves are summarized in simple distribution tables. Standard deviations and coefficients of variation are given in Table X for the older group of 50 subjects. These calculations were not made for the younger group of 50 subjects, but no great difference would be expected since the distribution tables for the two groups are similar. These calculations were only made for the R, S, and T waves since the measurements of P, Q, and S–T segment deviation were too small.

The P Wave

The height of the P wave (Table I) was measured to the nearest 0·5 mm. and the iso-electric line between the T and P waves was used as the reference level. The height was nearly constant in all chest positions (Fig. 1) but slightly less in C1 and C7. The P wave was most pointed in C1. The

TABLE I

Height of P Wave in Healthy Subjects

Height of P in mm.	CR (100 cases)							V (100 cases)							CF (50 cases)						
	Chest positions							Chest positions							Chest positions						
	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
3·0	—	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
2·5	—	0	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
2·0	5	5	10	10	10	10	5	1	1	—	—	—	—	—	—	1	—	—	—	—	—
1·5	12	17	25	27	23	23	18	2	2	4	1	1	2	—	—	—	1	—	—	—	—
1·0	73	73	61	62	65	66	73	20	26	30	29	27	25	13	3	2	3	2	1	1	—
0·5	9	4	3	1	2	1	4	63	63	59	66	67	66	73	4	10	9	9	8	8	7
0	1	—	—	—	—	—	—	1	4	7	4	5	7	14	2	6	12	25	27	22	8
−0·5	—	—	—	—	—	—	—	6	2	—	—	—	—	—	5	9	12	10	10	15	23
−1·0	—	—	—	—	—	—	—	7	2	—	—	—	—	—	24	16	10	4	4	4	12
−1·5	—	—	—	—	—	—	—	—	—	—	—	—	—	—	5	4	3	—	—	—	—
−2·0	—	—	—	—	—	—	—	—	—	—	—	—	—	—	7	2	—	—	—	—	—
Mean height	1·0	1·1	1·2	1·2	1·2	1·2	1·1	0·5	0·6	0·6	0·6	0·6	0·6	0·5	−0·8	−0·4	−0·2	−0·1	−0·1	−0·2	−0·4

In Tables I to IX the figures indicate the number of subjects.

duration of the P wave was about the same in right and left chest leads as in lead II. Graybiel (1944) found that the duration in lead II varied from 0·02 to 0·15 sec. with the majority less than 0·1 sec. The duration of the P wave in V chest leads was often slightly shorter than in CR. The P wave was bifid (Fig. 1) in 17 subjects, most commonly in right chest leads and the first peak was usually larger than the second. A bifid P wave was more frequent in chest leads than in limb leads. It was absent from the limb leads if found only in C1 to C3 and it was more frequent in CR than in V or CF leads.

In CR leads P was never negative, seldom over 2 mm. high, but once 3 mm. in CR2, never diphasic, and not flat, except once in CR1. In V1 and V2 the P wave was sometimes 1 mm. negative, and it was diphasic in V1 in 18 subjects and in V2 in six. In V3 to V7 the P wave was iso-electric or positive, and rarely over 1 mm. high. The P wave in CF leads was often negative, especially in CF1 and CF2.

The P–R interval was measured from the onset of P to the onset of QRS, and it was approximately the same length in lead II as in chest leads whether on the right or left. It was within the normal limits of 0·12 to 0·20 sec. (White, 1944), except once, when it measured 0·28 sec., and similar values have been found in health by Graybiel and others (1944), and Stewart and Manning (1944). Depression of the P–R segment was usually associated with S–T segment depression, and it is considered

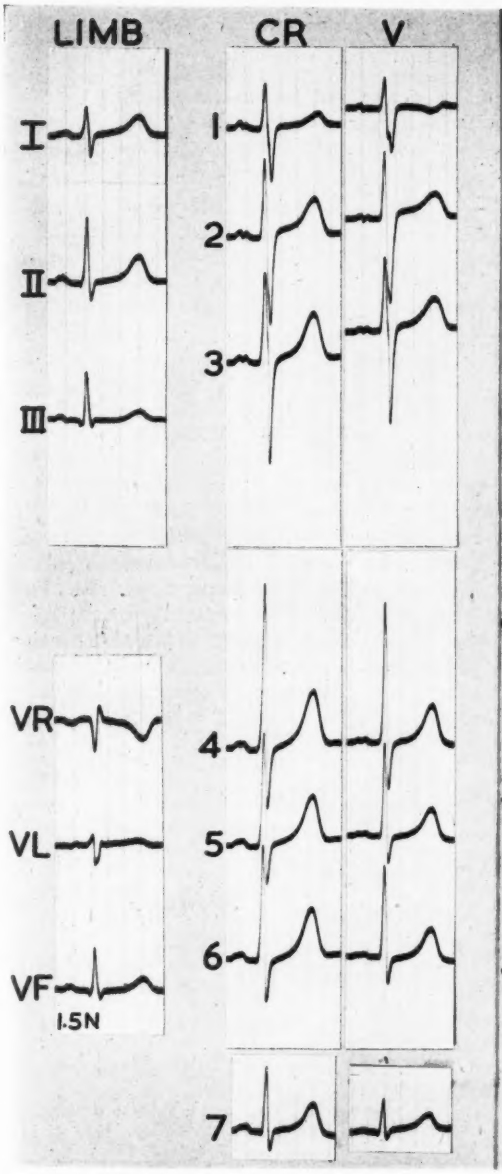

FIG. 1.—Bifid P waves in a man of 20 years. In this and subsequent records the time interval is 1/10 sec., and standardization is normal unless shown to be otherwise.

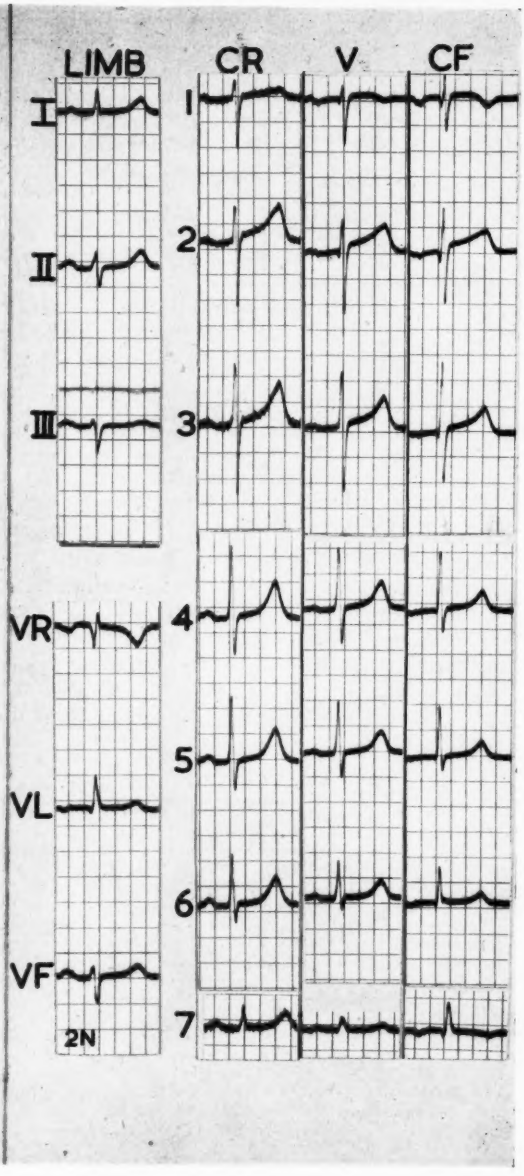

FIG. 2.—In this man of 71 years there is a small downward deflection in V1 and V2 preceded by a minute initial upward deflection. In CF1, CF2, and CF3 there were small Q waves. In CR1, CR2, and CR3 there were no deflections before the R wave.

under that heading, but, in three instances, P–R depression of 0·5 mm. was found in CR2 and CR3, and to a less extent in V2 and V3; it was then associated with S–T elevation.

The Q Wave

The depth of the Q wave (Table II) was measured to the nearest 0·5 mm.; the smallest Q was regarded as 0·25 mm. deep. The Q wave never exceeded 4 mm. in leads C1 to C7 with any indifferent electrode. In right chest leads (C1 to C3) of the usual pattern with S greater than R there

TABLE II

Depth of Q Wave in Healthy Subjects

Depth of Q in mm.	CR (100 cases)							V (100 cases)							CF (50 cases)						
	Chest positions							Chest positions							Chest positions						
	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
4	—	—	—	—	—	—	—	—	—	—	—	—	1	—	—	—	—	—	1	1	3
3–4	—	—	—	2	7	7	3	—	—	—	—	1	0	—	1	—	—	1	0	1	3
2–3	—	—	1	10	14	19	15	—	—	—	3	15	15	4	0	1	—	1	3	3	10
1–2	—	—	0	18	35	34	34	—	—	—	21	28	35	35	1	1	2	9	10	14	14
0–1*	—	1	7	26	16	21	36	1	2	3	14	27	33	52	0	0	0	3	14	12	8
0	100	99	92	44	28	19	12	99	98	97	62	29	16	9	48	48	48	36	22	19	12

* Measurements which are a whole number are placed in the range starting with that number, e.g. a subject with a Q of 1 mm. is placed in the 1–2 mm. range.

was never a Q in CR leads, and it was rare or small in V and CF leads. In left chest leads (C5 to C7) a small Q with tall R wave was the rule, but Q was absent in all CR leads in 12 per cent, V in 9 per cent, and CF in 14 per cent, mainly in the older age group; it was never entirely absent from all three series of chest leads in any one person. When a Q appeared in a left chest lead it became more obvious in leads farther to the left, and only disappeared in two subjects in CR and V leads, and in five in CF, but in all these the voltage of R was very low. The depth of Q decreased in some left leads C6 and C7 when there was a general decrease in voltage; the Q/R ratio (Table III),

TABLE III

Relation of Depth of Q to Height of R (Q/R ratio). Q is Expressed as a Percentage of R

Q/R ratio	CR (100 cases)							V (100 cases)							CF (50 cases)						
	Chest positions							Chest positions							Chest positions						
	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
100+	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	16
80–100	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
60–80	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	2
40–60	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1	5
35–40	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
30–35	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1	2
25–30	—	—	—	—	—	—	1	—	—	—	—	—	—	6	1	—	—	—	—	3	3
20–25	—	—	—	—	—	—	2	—	—	—	—	2	1	14	—	1	—	—	1	1	2
15–20	—	—	—	—	2	5	7	—	—	—	—	1	7	10	—	1	—	—	1	2	—
10–15	—	—	1	3	8	11	21	—	—	—	3	11	15	30	—	—	—	—	6	9	5
5–10	—	—	—	14	28	37	40	1	—	—	12	27	38	28	—	—	2	8	9	10	1
1–5	—	1	7	39	34	28	17	—	2	3	24	30	22	3	—	—	—	6	11	4	1

however, increased or remained approximately the same from right to left, and Q never exceeded 15 per cent of R in C4, and 30 per cent of R in CR5 to CR7, V5 to V7, and in CF5. Myers (1947) found this figure to be 25 per cent for V1 to V6.

Q waves occurred with about the same frequency in CR and V leads. They tended to be slightly

larger in CR because of the higher voltage, but the Q/R ratio was a little larger in V. In V leads from the right chest when the S wave was greater than the R wave a Q of 0·25 mm. appeared in three young adults; this was never found in CR leads. In two of these the small Q disappeared in V4 to reappear in leads farther to the left, while in the third the Q was found in all V chest leads. In another subject, aged 71 years, a small downward deflection was preceded by a minute initial upward deflection in V1 and V2 (Fig. 2). In CF leads the right chest pattern was modified by Q waves of from a half to three and a half millimetres in four subjects (Fig. 2). In CF6, Q was 50 per cent of R in one subject, and in CF7, 100 per cent or more of R in 16 subjects (Fig. 3), giving Q/R ratios of 50 and 100 per cent or over, respectively.

The width of the Q measured about 0·02 sec., and was always less than 0·04 sec., as found by Goldberger (1947). There was no difference between the width of Q in CR, CF, and V leads if the depth was comparable. The width of the QRS was found by Myers and others (1947) to range from 0·058 to 0·092 in V1, 0·064 to 0·098 in V2., 0·059 to 0·089 in V5, and 0·062 to 0·098 in V6. The Q–T interval was not measured for each case because, in those examined, it did not differ significantly from published observations on the limb leads (Ashman, 1942; Graybiel and others, 1944; Stewart and Manning 1944).

The R Wave

The QRS complex of the chest lead electrocardiogram has two distinct patterns (Groedel, 1933). Leads taken over the right ventricle consist of a small r and deep S (rS pattern) while leads over the left ventricle have a small q tall R, and small or absent s (qRs pattern). Chest leads 1 and 2 usually show the right pattern, 5, 6, and 7, the left pattern, while leads 3 and 4 may be either pattern or a mixture of the two (Fig. 4); obviously there is no constant pattern for individual chest positions because the relationship of the heart to the chest wall is variable. Myers (1947) found no R in V1 in 4, and in V2 in 2, out of 25 healthy subjects. In the present series the R wave in C1 was often small (Table IV) but it was never absent in CR or V. From right to left there was usually a progres-

TABLE IV

Height of R Wave in Healthy Subjects

Height of R in mm.	CR (100 cases)							V (100 cases)							CF (50 cases)						
	Chest positions							Chest positions							Chest positions						
	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
55–60	—	—	—	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
50–55	—	—	—	2	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
45–50	—	—	—	3	—	1	—	—	—	—	1	—	—	—	—	—	—	—	—	—	—
40–45	—	—	1	4	4	1	—	—	—	—	1	—	—	—	—	—	—	2	—	—	—
35–40	—	—	0	6	7	2	—	—	—	—	1	1	1	—	—	—	—	1	—	—	—
30–35	—	—	3	9	9	8	1	—	—	1	9	5	2	—	—	—	—	3	1	—	—
25–30	—	—	2	25	15	9	0	—	—	2	7	5	2	—	—	—	—	4	0	1	—
20–25	—	—	12	14	25	28	3	—	—	1	25	17	7	1	—	—	1	11	5	2	—
15–20	—	6	19	22	26	24	20	—	—	8	23	29	16	0	—	—	1	12	6	3	—
10–15	1	24	27	11	10	23	45	—	13	31	19	28	41	8	—	4	12	1	14	9	2
9–10	2	11	9	0	2	1	10	—	6	7	2	5	8	3	—	1	2	4	5	0	0
8– 9	1	9	4	3	0	2	3	—	11	5	3	5	12	11	—	3	2	4	4	2	0
7– 8	2	10	7	—	2	0	8	3	11	13	6	2	7	10	—	5	4	4	4	11	1
6– 7	9	7	5	—	—	1	6	3	18	7	3	2	2	9	2	9	1	1	5	3	3
5– 6	13	9	3	—	—	—	1	6	7	8	—	1	1	29	1	2	5	1	3	3	2
4– 5	20	8	2	—	—	—	2	14	8	6	—	—	1	7	3	7	5	2	0	5	5
3– 4	19	7	4	—	—	—	1	23	10	6	—	—	—	14	9	6	10	—	3	6	5
2– 3	22	6	1	—	—	—	—	32	12	4	—	—	—	6	14	7	5	—	—	3	10
1– 2	11	3	1	—	—	—	—	16	3	0	—	—	—	1	18	5	2	—	—	2	11
0– 1	—	—	—	—	—	—	—	3	1	1	—	—	—	1	2	1	—	—	—	—	5
0	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1	—	—	—	—	—	6
Mean height	3·8	8·0	13·3	24·5	22·6	20·0	12·0	2·9	6·1	9·4	18·7	16·5	13·3	5·9	2·2	5·0	6·8	14·4	11·4	8·0	2·9

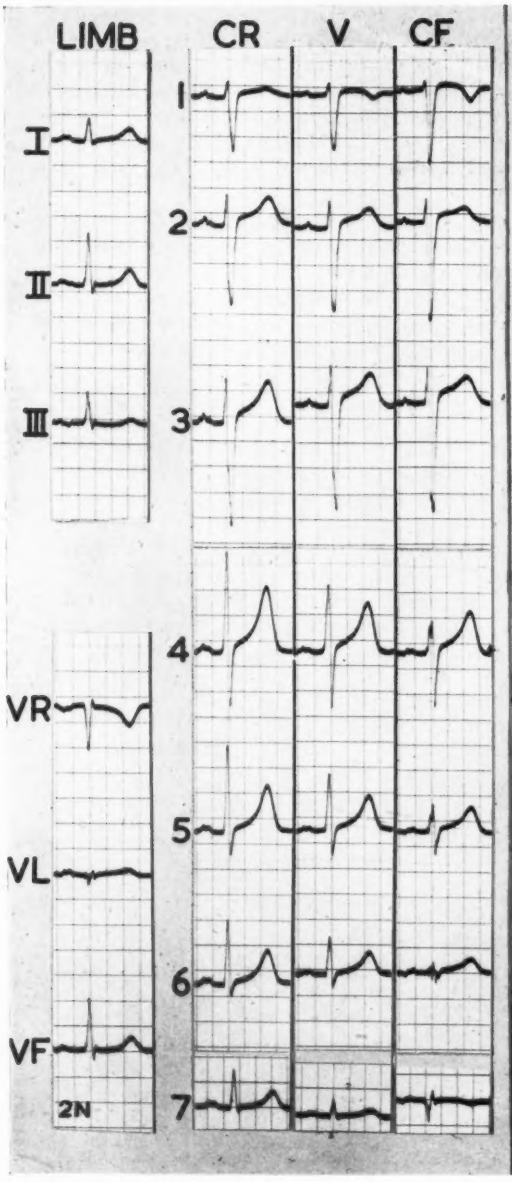

FIG. 3.—The Q wave is relatively large in CF7.

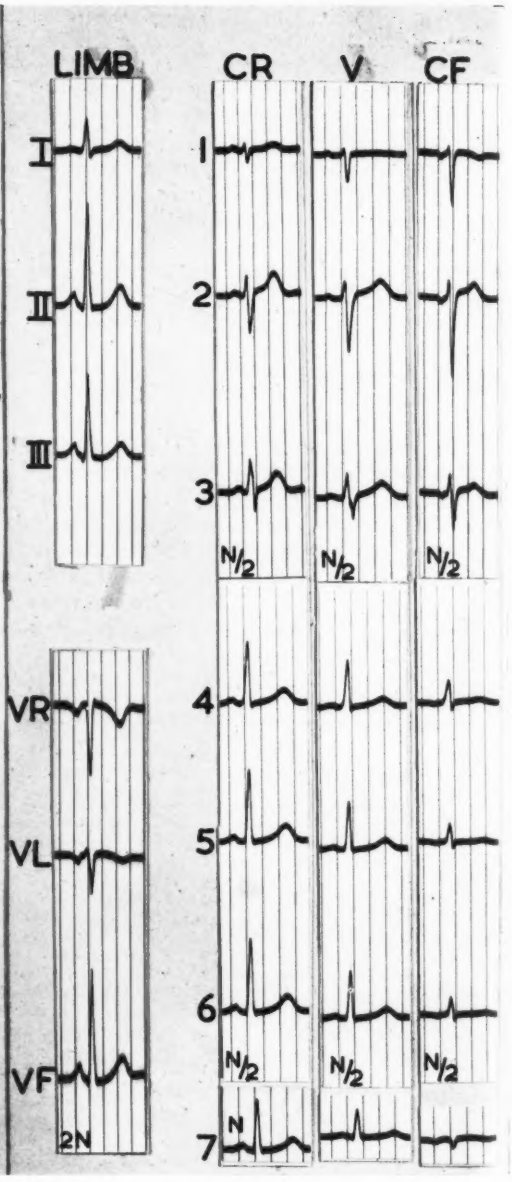

FIG. 4.—In this man of 44 years chest leads 1 and 2 show the right pattern, leads 4, 5, 6, and 7 show the left pattern, while 3 is intermediate. There is no Q wave until C7.

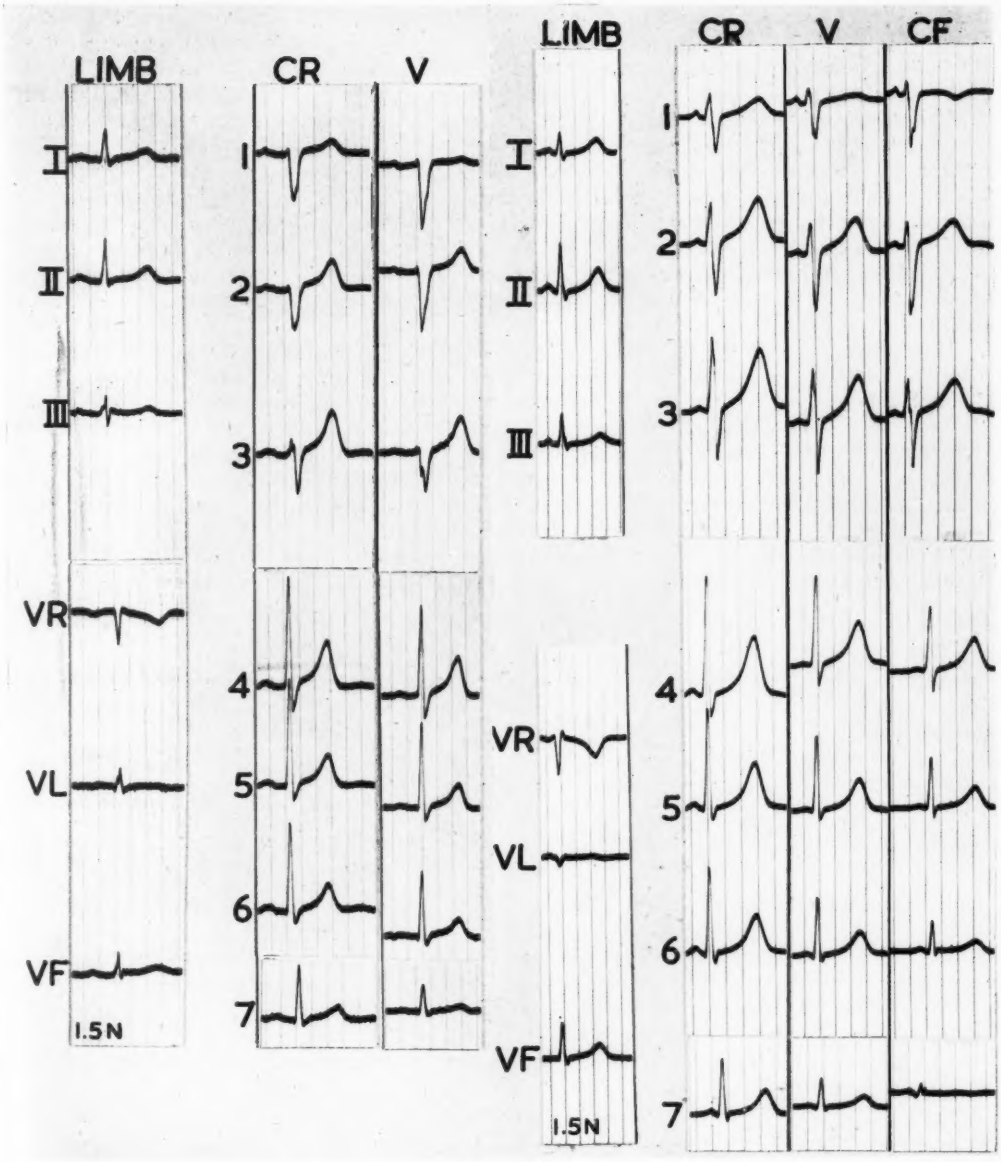

FIG. 5.—The R wave is the same height in V1, V2, and V3, in this man of 34 years.

FIG. 6.—Slurring of R or S in leads from the right chest and transitional zone in this man of 21 years.

sive increase in the height of the R wave to a peak in C4, sometimes in C3, C5, or C6 decreasing in size again in leads farther to the left. In a few instances the R wave was the same height in several chest leads, for example, in V1, V2, V3 (Fig. 5); rarely the R wave fell 1 or 2 mm. in a lead farther to the left, but this might have been due to respiratory variation. There were no significant differences in the size of R in the two age groups. Slurring of any part of R or S occurred in leads from the right chest or transitional zone (Wilson, 1947), as in Fig. 6, but not in leads from the left chest showing a qRs pattern in this investigation. A second R wave (R′) following the S was quite common in leads from the right chest, particularly at a high level (Fig. 9). An R′ wave in C1, or in C1 and C2, was found in 11 subjects (Fig. 7 and 10). The R′ was small and less than R except when carried higher by S–T elevation in one instance, and in CF1 only in another; in these subjects there was no slurred S in standard lead 1 or chest lead 7, while in a 21-year-old medical student, S was slurred in I, II, and C5 and C6, not in C7; but there was no R′ in C1. In one otherwise healthy man aged 41 years the R′ in C1 was slightly taller than R and was associated with a slurred S in leads I and C4 to C7; he was considered to have partial right bundle branch block and was excluded from the series.

The R wave varied in height with the indifferent electrode and was tallest in CR, intermediate in V, and shortest in CF leads, with one exception where the R wave measured 1 mm. in CR1 to CR3 and 1·5 mm. in V1 to V3 (Fig. 8) and several exceptions in right CF leads. In CR4 the R wave varied in height from 8 to 60 mm. with an average of 25 mm., and in V4 from 6 to 50 mm. with an average of 19 mm. These values are higher than those found by Myers (1947), namely R in V4 from 2 to 25 mm., average 13·0 mm. in 52 subjects, and by Dolgin (1949), namely R in V4 from 5·8 to 27·1 mm., average 14·6 mm. in 44 subjects. In CF4 the R wave varied from 4 to 45 mm., and Katz (1946) suggested a minimal normal value of 3 mm. for this lead.

The division of chest leads into two main patterns, rS on the right and qRs on the left, is seen by examining the ratio of R to S (Table V). The clearest division took place in V leads. The R wave

TABLE V

RATIO OF R TO S IN HEALTHY SUBJECTS

R/S ratio	CR (100 cases)							V (100 cases)							CF (50 cases)						
	Chest positions							Chest positions							Chest positions						
	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
R>S	6	15	50	95	98	99	99	0	5	21	90	97	99	99	1	0	6	41	49	44	37
R=S	4	5	2	1	0	0	0	0	0	6	1	1	0	0	0	0	2	3	0	2	6
R<S	90	80	48	4	2	1	1	100	95	73	9	2	1	1	49	50	42	6	1	4	7

was always less than the S wave in V1, and was greater than S in V7 in all but one subject with a long narrow heart on radiological examination. In CR1 there were more exceptions for R was greater than S in six subjects (Fig. 9), but in most of these the voltage was low. In CR7 there was only one subject with S greater than R, the same as in V7.

In children the R/S ratio in right chest leads is different from adults, for the R wave is often greater than the S wave in V1 or V2 (Fig. 11 and 12, p. 224), and there may be steep T inversion in these leads (Master, 1937; Suarez, 1946). Left chest leads in children are similar to those in adults.

THE S WAVE

An S wave (Table VI) was present in right chest leads C1 to C3, with one exception in CF1; it was greater than R in most subjects, and always so in V1. It usually reached its maximum depth in C2 but not till C3 in about one-third of the older and one-sixth of the younger group, and in CR4 and CF4 in one subject. The S wave was deep in some subjects, reaching a maximum of 35 mm. in CR and V, and 40 mm. in CF leads. It diminished progressively to the left, but occasionally

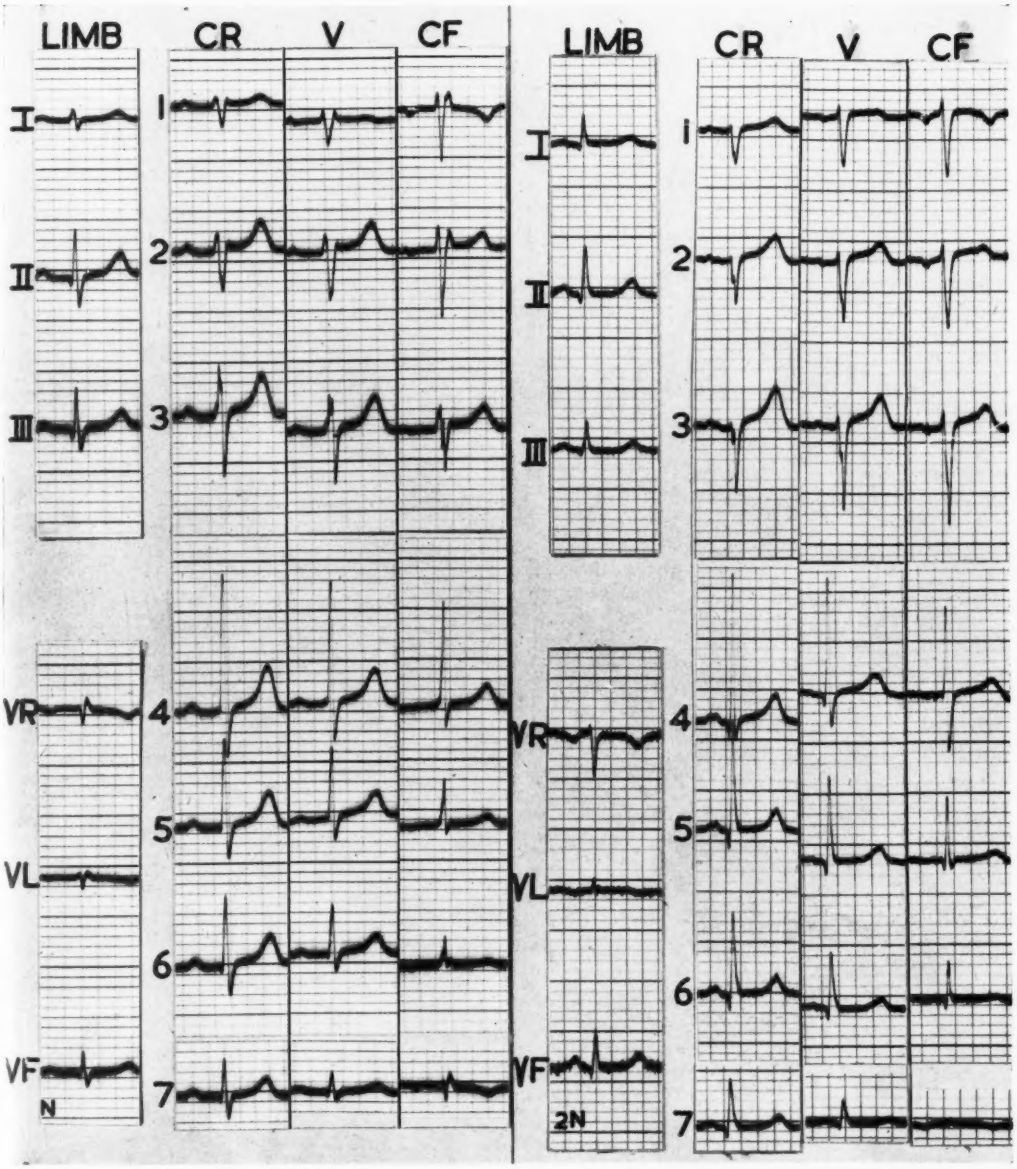

FIG. 7.—R′ in C1 and C2 in this man of 41 years.

FIG. 8.—The R wave was usually tallest in CR leads, intermediate in V, and shortest in CF, but in this man, aged 59 years, R was shortest in CR1, CR2, and CR 3.

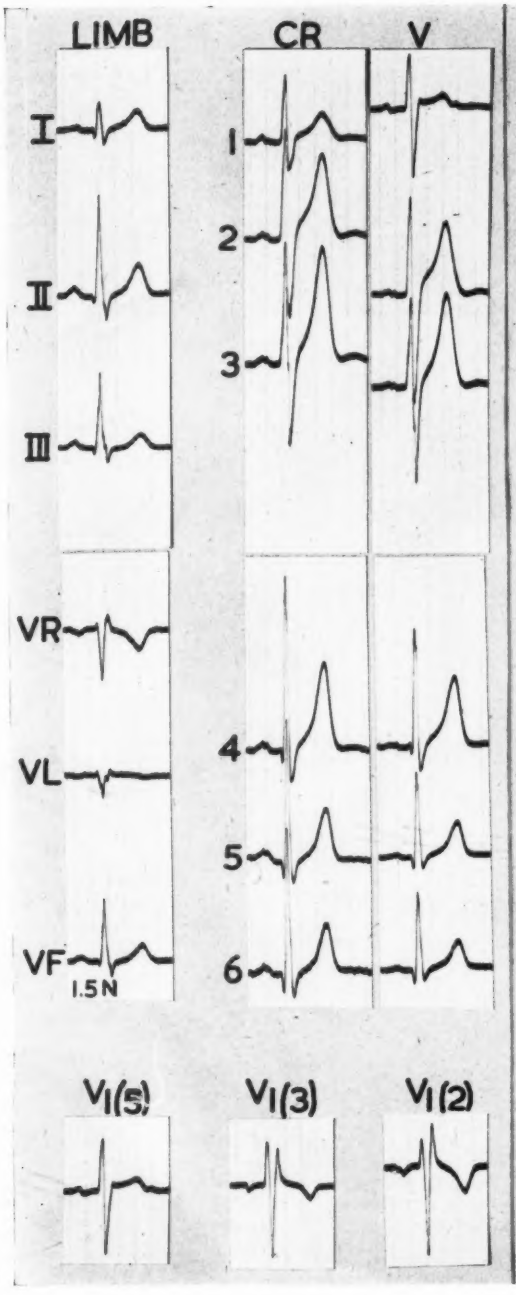

FIG. 9.—In this man of 24 years (not in the series) R is greater than S in CR1, but not in V1. There is an R′ in V1 taken in the second and third intercostal spaces, but it is very small in standard V1, or in V1 in the fifth space.

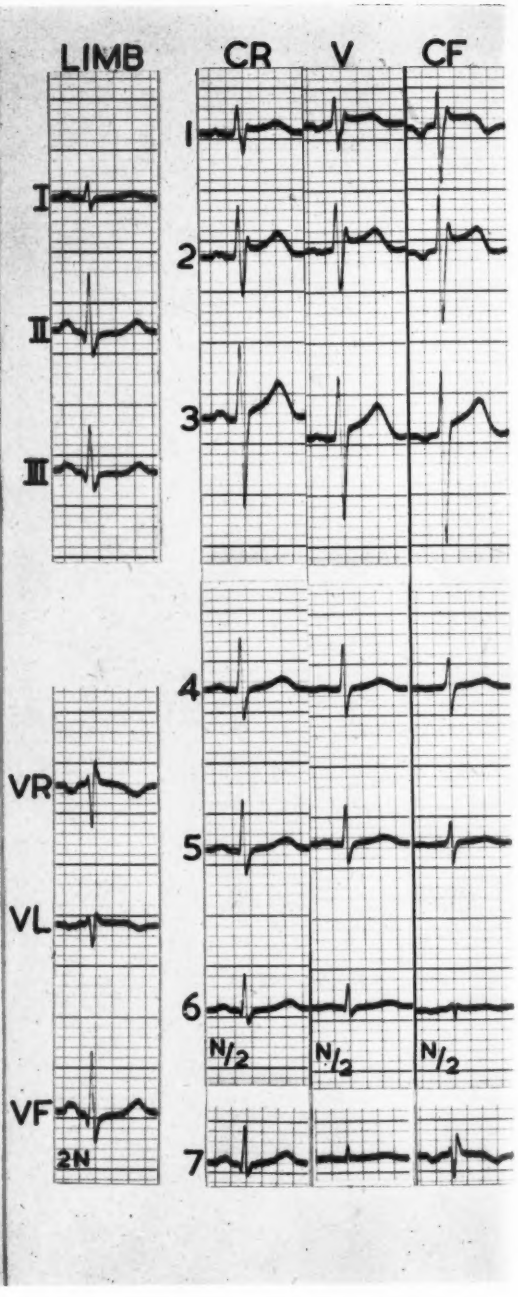

FIG. 10.—S–T elevation in leads from the right chest in a man of 61 years. There is an R′ in C1 and C2.

remained at the same height and rarely increased slightly though by less than 1 mm. In left chest leads S was comparatively small and often absent, but once in CR6 and CR7, once in V6 and V7, and often in CF6 and CF7, it was greater than R.

In right chest leads S was deepest in CF, intermediate in V and least deep in CR, but in left chest leads S was often deepest in CR.

TABLE VI

DEPTH OF S WAVE IN HEALTHY SUBJECTS

Depth of S in mm.	CR (100 cases)							V (100 cases)							CF (50 cases)						
	Chest positions							Chest positions							Chest positions						
	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
35–40	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1	—	—	—	—	—
30–35	—	1	—	—	—	—	—	—	2	—	—	—	—	—	—	1	—	—	—	—	—
25–30	—	1	3	—	—	—	—	1	2	4	—	—	—	—	1	1	4	—	—	—	—
20–25	—	6	10	—	—	—	—	0	18	13	—	—	—	—	7	13	6	—	—	—	—
15–20	3	30	16	2	1	—	—	14	31	21	1	—	—	—	11	15	11	2	—	—	—
10–15	28	35	37	18	1	1	—	37	26	32	15	—	—	—	19	13	14	9	—	—	—
5–10	53	27	27	37	17	7	1	40	20	26	41	12	2	—	9	5	15	16	11	2	—
4–5	10	—	3	12	13	4	1	7	1	1	10	13	1	—	2	0	—	10	5	4	2
3–4	1	—	2	9	19	17	1	1	—	1	12	14	10	—	—	1	—	3	6	3	1
2–3	5	—	2	11	14	26	15	—	—	2	10	27	20	2	—	—	—	7	13	10	4
1–2	—	—	—	6	20	20	43	—	—	—	6	16	39	35	—	—	—	1	8	16	9
0	—	—	—	5	15	25	39	—	—	—	5	18	28	63	1	—	—	2	7	15	34
Mean depth	7·8	13·1	12·6	6·1	3·0	2·0	0·8	10·1	14·9	13·3	5·8	2·5	1·3	0·2	13·3	16·7	14·4	6·0	2·9	1·5	0·5

S–T DEVIATION

The level of the S–T segment was taken 1 mm. after the termination of the QRS complex, and its deviation from the iso-electric line (T–P interval) was measured to the nearest millimetre (Table VII). Deviation of less than 0·5 mm. was not noted.

TABLE VII

S–T DEVIATION IN HEALTHY SUBJECTS

S–T deviation in mm.		CR (100 cases)							V (100 cases)							CF (50 cases)						
		Chest positions							Chest positions							Chest positions						
		1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
S–T elevation	+3	—	1	1	—	—	—	—	—	2	1	—	—	—	—	—	—	—	—	—	—	—
	+2	—	7	6	6	3	2	1	—	8	7	4	1	—	—	2	6	4	1	1	—	—
	+1	39	64	48	29	19	16	5	48	65	56	28	12	9	3	34	34	28	17	5	6	1
	0	57	23	40	59	73	77	90	52	24	32	63	83	88	95	14	10	18	32	44	44	49
S–T depression	−1	4	5	4	4	4	4	4	—	1	4	5	4	3	2	—	—	—	—	—	—	—
	−2	—	—	1	2	1	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—

S–T *elevation* (Fig. 10) was found frequently in leads from the right chest especially with high voltage and it reached 3 mm. in two subjects. It was about the same for CR and V leads, but was less in CF. In shape the raised S–T segment was straight or concave upwards ending in an upright T wave, in CR and V leads, as pointed out by Myers (1947).

S–T *depression* was much less common and it varied with the indifferent electrode employed. It was greatest in CR leads reaching 2 mm. in two young women with tachycardia (rates 120 and

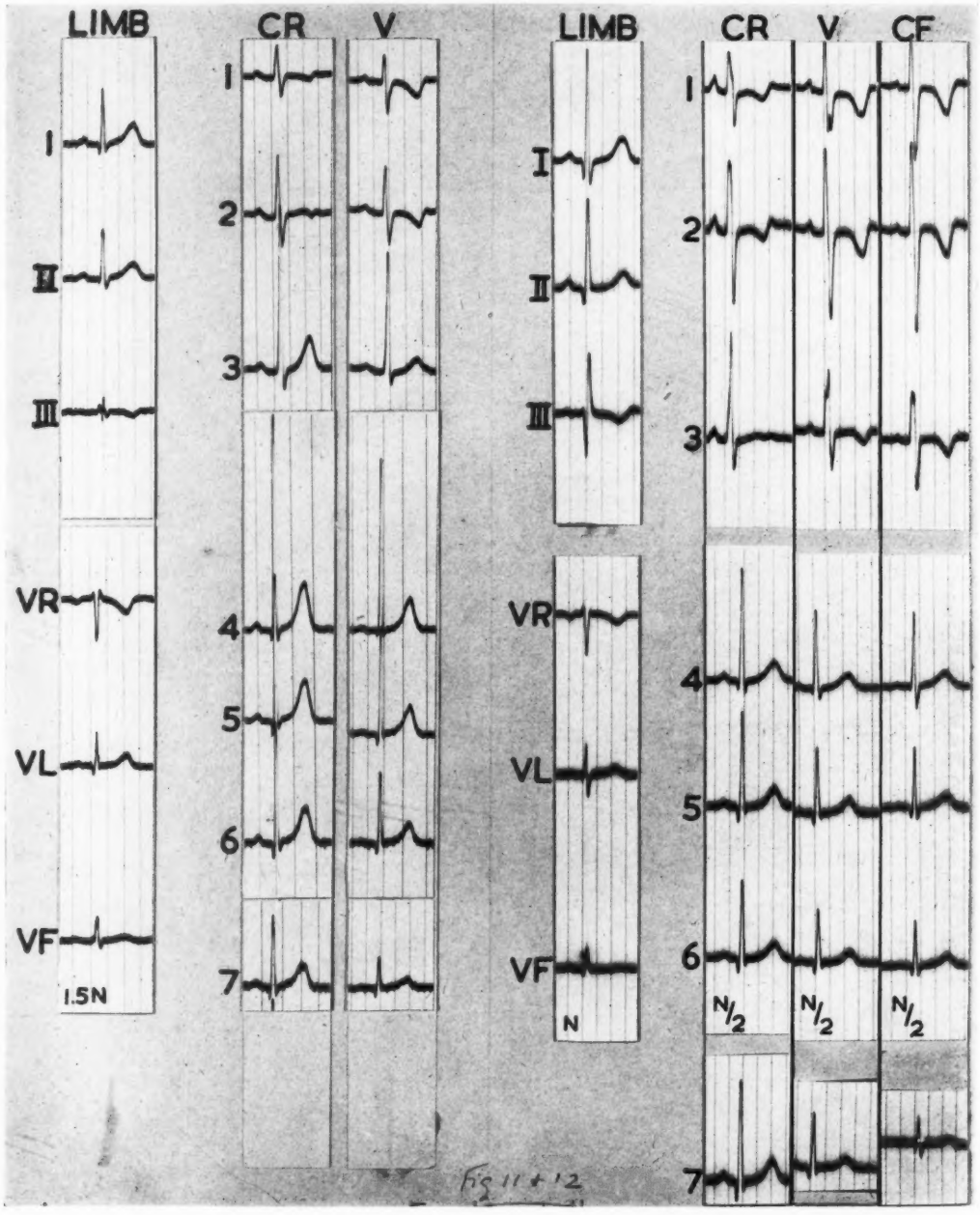

FIG. 11 and 12.—R is equal or larger than S with steep T inversion in C1 and C2 in these children aged five years.

115 a minute) and depression of the P–R interval (Fig. 13). With a short diastole the P wave fell on the descending limb of the preceding T wave so that the T–P interval was raised causing apparent depression of the P–R and S–T segments in relation to the T–P reference level. S–T depression of 0·5 to 1·0 mm. in CR leads was found in six subjects chiefly affecting the left chest leads; in four there was tachycardia and consequent P–R depression also; in two the S–T depression was accompanied by slight P–R depression without tachycardia. In V leads S–T depression not exceeding 1·0 mm. was found in five subjects of whom four had tachycardia with P–R depression, and one slight P–R and S–T depression without tachycardia. In CF leads S–T deviation was minimal, for similar deviation at the left foot (VF in Fig. 13) cancelled out changes at the chest electrode. These changes agree with those found by Myers (1947) who stated that depression of the RS–T junction was very rare in the præcordial leads in health and that it should be regarded as abnormal if it was 0·5 mm. or greater, provided that tachycardia or a prominent auricular T wave was absent.

The T Wave

In right chest leads the T wave was sometimes very tall reaching 18 mm. in CR, 16 mm. in V, and 15 mm. in CF (Table VIII), it was often taller than the R wave. In left leads of qR or qRs pattern the T averaged about one-quarter of the height of R for any of the indifferent electrodes. With a

TABLE VIII

Height of T Wave in Healthy Subjects

Height or depth of T in mm.	CR (100 cases)							V (100 cases)							CF (50 cases)						
	Chest positions							Chest positions							Chest positions						
	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
18–	—	1	2	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
17–18	—	0	2	1	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
16–17	—	1	3	1	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
15–16	—	4	1	3	0	—	—	—	1	—	—	—	—	—	—	—	—	—	—	—	—
14–15	—	3	4	3	0	—	—	—	1	2	1	—	—	—	—	—	1	—	—	—	—
13–14	—	5	5	2	0	—	—	—	2	2	0	1	—	—	—	3	0	—	—	—	—
12–13	—	2	8	6	1	3	—	—	2	5	3	0	—	—	—	0	0	1	—	—	—
11–12	—	8	6	4	3	0	—	—	5	5	4	1	—	—	—	0	3	0	—	—	—
10–11	—	7	8	8	4	5	—	—	8	10	3	0	—	—	—	2	3	1	—	—	—
9–10	—	8	11	6	8	5	—	—	5	9	3	0	1	—	—	1	3	2	1	—	—
8–9	3	14	14	16	8	3	—	—	9	6	10	3	1	—	—	5	5	3	1	—	—
7–8	1	8	10	14	16	6	1	1	9	11	9	6	4	—	—	4	6	3	0	—	—
6–7	4	12	12	9	18	18	2	2	12	19	19	17	6	—	—	9	3	5	3	1	—
5–6	9	13	5	9	10	17	15	7	10	11	14	13	7	—	—	5	7	8	5	3	—
4–5	18	10	5	10	13	19	15	3	15	13	12	21	18	—	1	4	9	12	7	2	—
3–4	20	3	3	5	10	15	26	9	12	2	13	16	24	6	3	3	7	7	10	2	—
2–3	27	0	0	2	7	9	34	19	7	4	7	17	31	28	5	11	1	2	12	14	1
1–2	17	1	1	1	—	—	7	29	2	1	2	5	8	57	4	0	1	6	10	21	4
0·5–1	1	—	—	—	—	—	—	3	—	—	—	—	—	7	0	1	0	—	0	3	3
0	—	—	—	—	—	—	—	8	—	—	—	—	—	1	2	0	1	—	1	2	8
−0·5–1	—	—	—	—	—	—	—	4	—	—	—	—	—	1	1	0	—	—	—	1	9
−1–2	—	—	—	—	—	—	—	15	—	—	—	—	—	—	19	1	—	—	—	1	20
−2–3	—	—	—	—	—	—	—	—	—	—	—	—	—	—	11	1	—	—	—	—	4
−3–4	—	—	—	—	—	—	—	—	—	—	—	—	—	—	3	—	—	—	—	—	0
−4	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1	—	—	—	—	—	1
Mean height ..	3·5	8·2	9·2	7·9	6·3	5·4	3·3	1·5	6·5	7·1	5·8	4·4	3·4	1·5	0·6	5·3	6·0	4·7	3·3	1·7	−0·5

general decrease in voltage as may occur from C5 to C6 and C7 the T/R ratio remained about the same. T was always more than one-twelfth and rarely exceeded three-quarters of R (Table IX) in left pattern CR and V leads with the exception of two subjects with flat or inverted T waves in V7. There was little difference in the T wave in the two age groups in CR leads, but in V1 the T was more often inverted in the younger group. In children the T is frequently inverted in C1 and other right

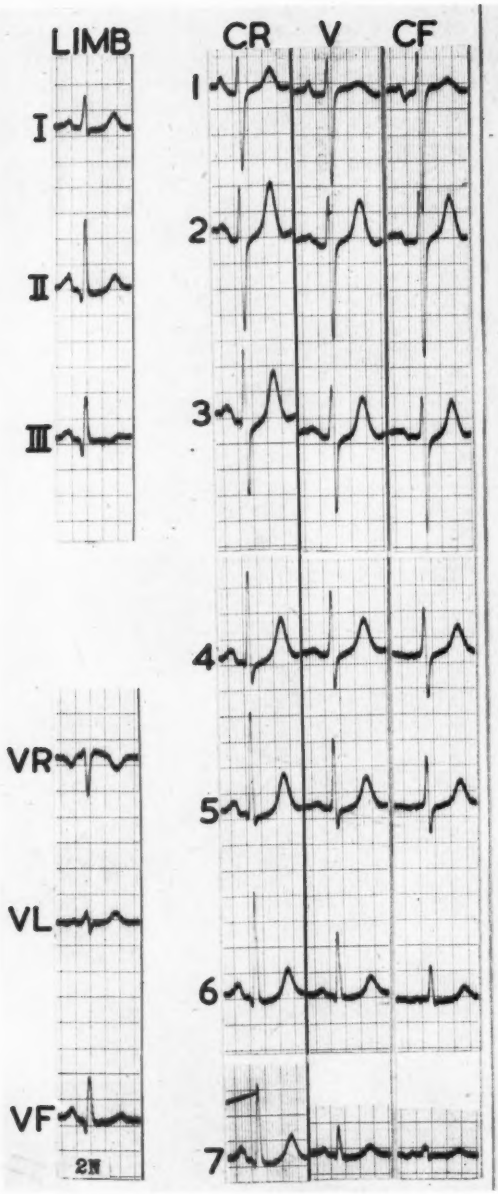

FIG. 13.—P–R and S–T depression from tachycardia (rate 120) in a pregnant woman aged 32 years.

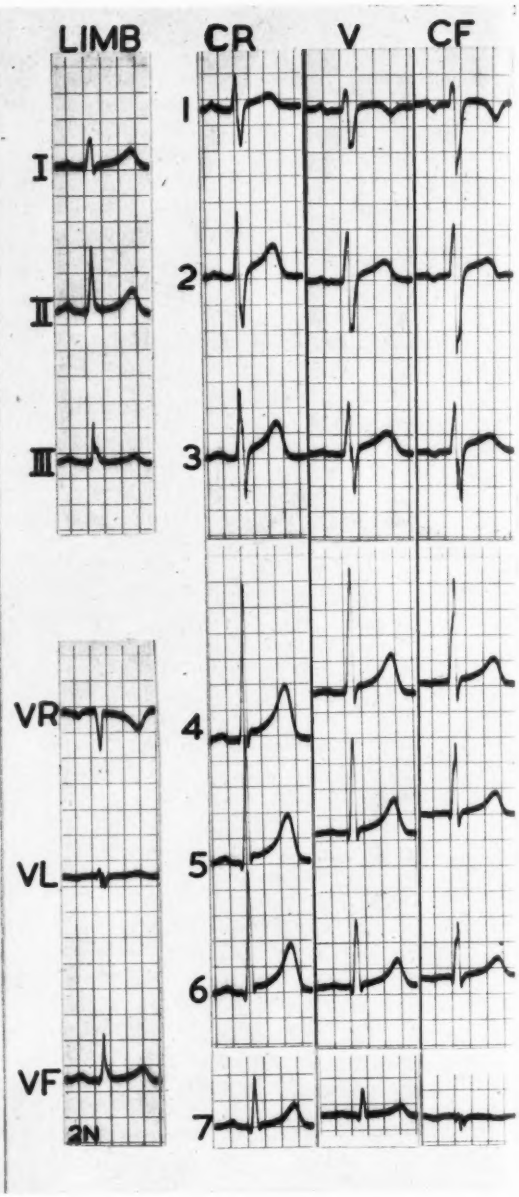

FIG. 14.—T wave inversion in V1 and in CF1, but not in CR1, in this man of 28 years.

chest leads (Fig. 11 and 12) as shown by Master (1937) and Suarez (1946). In shape the T wave showed a gradual rise with an upward concavity (Myers and others, 1947) to the peak when it fell steeply to the iso-electric level. It was symmetrical only in the few subjects showing S–T depression. Its peak was never bifid but in one man of 49 years it was flat.

The height of the T wave varied with the indifferent electrode and was greatest in CR, intermediate in V, and least in CF leads. From CR1 to CR7 the T wave was always upright in the 100

TABLE IX

RATIO OF HEIGHT OF T TO HEIGHT OF R (T/R RATIO) IN LEFT CHEST LEADS WHEN S IS LESS THAN ONE-QUARTER OF R AND T IS POSITIVE. T IS EXPRESSED AS A PERCENTAGE OF R

T/R ratio	CR (100 cases)				V (100 cases)				CF (50 cases)			
	Chest positions				Chest positions				Chest positions			
	4	5	6	7	4	5	6	7	4	5	6	7
90–100	—	—	—	—	—	—	—	1	—	1	—	—
80–90	—	—	—	—	—	—	—	1	—	0	—	—
70–80	—	—	—	1	—	—	—	0	—	0	1	—
60–70	1	3	—	2	—	—	—	1	—	1	0	—
50–60	2	2	2	10	2	2	2	3	—	0	1	—
40–50	4	6	11	11	2	6	7	14	—	3	1	—
30–40	19	19	15	14	11	15	17	17	2	5	3	2
20–30	23	27	32	28	16	21	22	30	4	6	6	2
10–20	12	22	23	28	9	26	33	24	4	6	10	1
9–10	1	2	0	—	—	1	—	0	—	1	0	0
8–9	2	1	2	—	—	1	—	2	—	1	3	1
7–8	—	—	—	—	—	—	—	—	—	1	1	—
6–7	—	—	—	—	—	—	—	—	—	0	0	—
5–6	—	—	—	—	—	—	—	—	—	1	1	—
4–5	—	—	—	—	—	—	—	—	—	—	1	—
Mean ratio ..	26	28	27	29	27	23	25	28	23	27	21	23

adults, but an isoelectric or slightly inverted T in CR1 occurs occasionally in younger adults. In left CR leads T was lowest in CR7 with a minimum height of 1 mm. but not low in relation to the R wave for it was never less than one-tenth of R. The T wave in V was always lower than in CR leads. It was inverted in V1 (Fig. 14) in 19 of the 100 subjects (12 in the younger group and 7 in the older), but it was always upright in V2; in every instance of T inversion in V1 a right pattern chest lead with S greater than or about equal to R with an upright T was found in V2. The T wave was upright in V2 to V6, but it was often low in V7 when R was low, and it was once flat (Fig. 15) and once inverted by 0·5 mm. In V6 the T was never less than 10 per cent of R, and in V7 with an upright T wave never less than 8 per cent of R. Myers (1947) found inversion of the T wave in VI in 7 of 16 cases, in V2 in three women aged 19, 31, and 45 years, out of 52 cases; he found a flat T in V3 once and in V6 once; he did not mention V7. In CF1 the T wave was inverted in 35 of the 50 subjects, in CF2 in two, and T was flat once in CF3. With one exception a right chest lead with S greater than R and upright T wave was found in CF3, if not in CF1, or CF2. The T wave was usually inverted in CF7, twice inverted in CF6 (Fig. 16), and once flat in CF5; it was always upright in CF4, but its inversion in health in this lead has been found by others (Sodeman, 1937; Graybiel, 1944; Katz, 1948).

COMPARISON OF CR, CF, AND V CHEST LEADS

While the British Cardiac Society have recently (1949) recommended the central terminal (V), there is still no universal agreement on any one indifferent electrode in chest lead electrocardiography and many clinicians may continue to use the chest lead to which they are most accustomed until another lead is shown to have practical advantages. Leaving theoretical considerations aside, the best chest lead is the one which varies least in health and shows the earliest changes in disease.

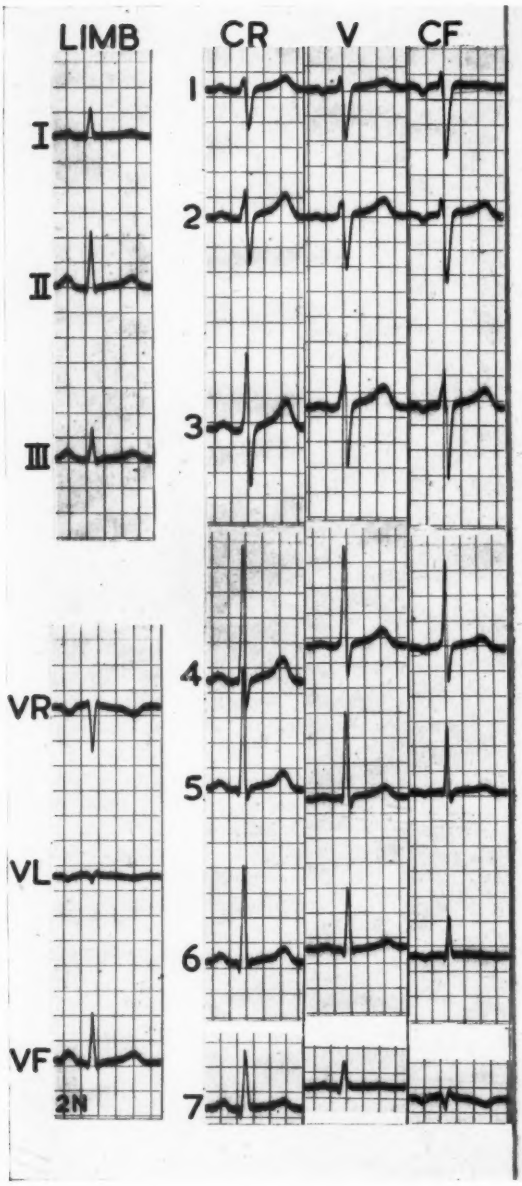

FIG. 15.—Flat T in V7 in a man of 62 years.

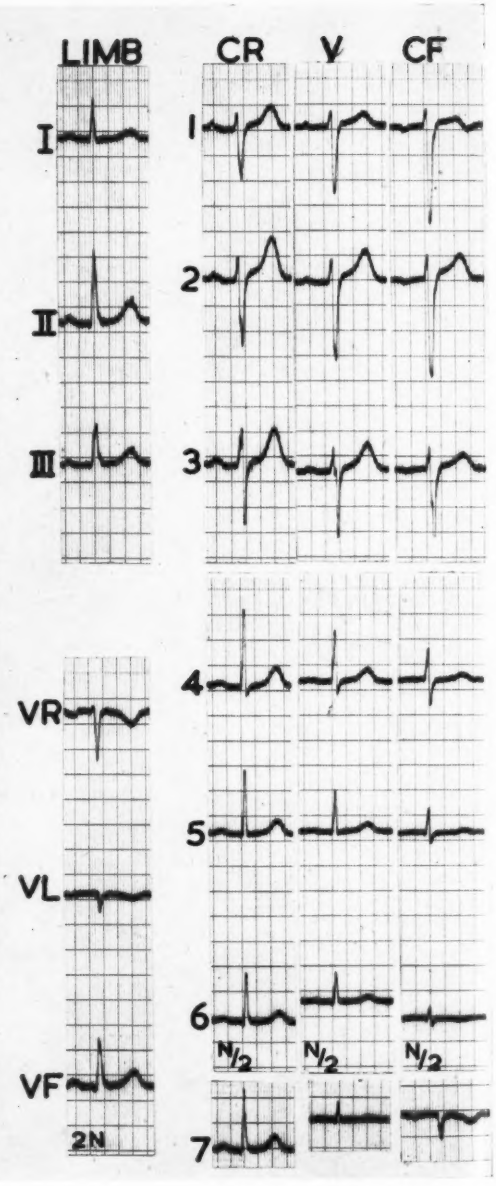

FIG. 16.—Low T wave in CF5 and inversion in CF6 and CF7 in a man of 45 years.

Normal variations in CF leads are very great, compared with those in CR and V leads. These variations are shown in Table X where the coefficients of variations for the R, and T waves in CF leads are usually much greater than in CR and V leads. Normal T wave inversion in CF leads is another disadvantage. CF leads are said to be more sensitive in detecting minor abnormalities from coronary artery disease, but it is probable that most of these minor abnormalities fall within their wide limits of normal variation. These are due to the great changes in potential at the indifferent electrode on the left foot with changes in position of the heart. They make CF leads unsuitable for routine use.

Chest leads would be truly unipolar if the indifferent electrode were at zero potential This has not yet been achieved (Eckey and Fröhlich, 1938) but the central terminal (V) is the nearest approach (Wilson, 1934; Burger, 1939). An equally good indifferent electrode for practical, though not for theoretical, purposes is one with a constant potential so that the same error is always introduced. The right arm indifferent electrode (CR) is a close approach to this. Whether the central terminal is less variable than the right arm has yet to be determined. Groedel (1948) believes that the central terminal is unduly influenced by the left foot which is so variable. In this investigation it was found that CR and V chest leads have very similar coefficients of variation for the R, S, and T waves (Table X) in most leads. V leads show less S–T segment deviation (Table VII) and a clearer division

TABLE X

MEAN VALUES, STANDARD DEVIATIONS, AND COEFFICIENTS OF VARIATION, FOR THE R, S, AND T WAVES OF 50 SUBJECTS OVER 40 YEARS OF AGE

Chest position	Mean			Standard deviation			Coefficient of variation		
	CR	V	CF	CR	V	CF	CR	V	CF
				R wave					
1	3·0	2·2	2·2	1·5	1·0	1·4	49	46	62
2	6·6	5·2	5·0	3·8	2·9	2·8	58	55	57
3	12·3	9·0	6·8	8·0	6·0	4·5	65	66	67
4	24·0	19·0	14·4	11·0	9·0	8·1	46	47	57
5	21·6	16·0	11·4	8·4	7·0	5·8	39	42	51
6	19·0	13·0	8·0	8·9	7·0	6·0	47	54	74
7	10·7	5·1	2·6	5·0	3·2	2·5	47	63	95
				S wave					
1	7·7	9·8	13·3	2·9	3·8	5·4	38	39	41
2	12·8	14·0	16·7	5·0	5·3	6·5	39	38	40
3	12·7	13·2	14·4	5·0	5·2	6·2	41	39	43
4	6·6	6·0	6·0	4·1	4·0	3·5	62	58	60
5	3·3	2·6	3·0	3·2	2·2	2·4	99	86	81
6	2·1	1·5	1·5	2·2	1·5	1·9	108	106	125
7	0·8	0·2	0·5	1·1	0·3	1·1	131	170	202
				T wave					
1	3·3	1·6	0·6	1·6	1·7	1·8	50	111	329
2	8·6	6·8	5·3	4·0	3·5	3·3	47	51	62
3	9·8	7·7	6·0	4·0	3·1	3·0	40	40	49
4	8·6	6·5	4·7	3·7	3·0	2·5	43	46	52
5	6·8	4·7	3·3	2·9	2·1	2·5	42	46	75
6	5·7	3·6	1·7	2·6	1·8	1·4	45	49	82
7	3·2	1·3	−0·5	1·4	0·8	1·1	43	61	206

into right and left patterns, but normal T wave inversion in V1, and rarely in V7, is perhaps a disadvantage. Thus neither lead has shown much advantage over the other in this investigation.

SUMMARY AND CONCLUSIONS

Standard limb leads, unipolar limb leads, and chest leads CR1 to CR7 and V1 to V7 were taken

in 100 healthy adults, and leads CF1 to CF7 were taken in the first 50 (older group). Measurements of the P, Q, R, S, and T waves, and of the S–T segment, together with Q/R, R/S, and T/R ratios are shown in simple distribution tables. Standard deviations and coefficients of variation are given for the R, S, and T waves in the older group of 50 subjects. The *extreme* limits for the electrocardiogram in health cannot be given from the examination of 100 subjects. The trend of the frequency distribution shows that the probability of a measurement falling much outside the range of these observations must be small.

The P wave which remained about the same height in leads C1 to C7 and was sometimes bifid, was most positive in CR leads, and was rarely more than 2 mm., or less than 0·5 mm. in height. In V1 and V2 P might be 1 mm. negative; in V3 to V7 it was isoelectric or positive, not exceeding 1·5 mm. in height. In CF leads P was usually isoelectric or negative.

The Q wave did not exceed 4 mm. with any indifferent electrode. In right chest leads when S was greater than R there was no Q wave except in rare instances in V leads when there was a Q of 0·25 mm., or in CF leads when it was slightly larger.

In left chest leads a Q wave was found in 90 per cent of persons examined, but it was less than one-seventh of R in C4, and one-third of R in C5 to C7, excepting CF6 and CF7. When a Q appeared in a chest lead its ratio to R increased in leads farther to the left, except in rare instances of very low voltage.

The R and S waves. The R wave was very small in right CR and V chest leads, but it was always present in this series. It increased in height, rarely remaining the same, in leads farther to the left to a peak usually at C4, then decreased again towards C7. The R wave was usually tallest in CR leads, intermediate in V, shortest in CF. The S wave was deepest in CF, intermediate in V, and least in CR, in right leads, but it was often deepest in CR in left leads. R was less than S in V1, and, with some exceptions, in CR1; R was greater than S in CR7 and V7 with one exception. In children R may be greater than S in C1 or C2 and there may be steep T inversion in these leads.

A second R wave sometimes occurred in C1 or C2, but it was small and less than the first R.

Slurring of R was not seen in left leads of qR or qRs pattern, but was frequent in right leads or in the transitional zone.

S–T elevation reached 3 mm. in leads from the right chest, especially with a high voltage S wave. In shape it was straight or concave upwards ending in an upright T wave in CR and V leads.

S–T depression greater than 0·5 mm. below the T–P level was not seen in chest leads in the absence of tachycardia and depression of the P–R segment or, more rarely, of P–R depression alone. S–T depression was greatest in CR, intermediate in V, least in CF leads.

The T wave was often very tall in right leads reaching 18 mm. in CR, 16 mm. in V, and 15 mm. in CF leads, often exceeding the R wave. In left leads the T averaged about one-quarter of the height of R and was never less than one-twelfth of R in CR and V leads, with rare exceptions in V7.

The T wave was most positive in CR leads, and was upright in the adults examined, but it is frequently inverted in CR1 in children. In V1 it was often inverted in adults, but a right pattern chest lead with S greater than R was then found in V2. In V2 to V6 the T wave was upright. In V7 the T wave was occasionally flat or slightly inverted. A flat or inverted T wave was found in any CF chest lead except CF4, and especially in CF1, CF2, and CF7.

A comparison of CR, V, and CF leads in health shows that CF is too variable to be recommended for routine use, while neither CR nor V leads have much practical advantage over each other provided that the normal pattern and variations of each are known.

I am grateful to Dr. William Evans, Physician to the Cardiac Department, and to Sir John Parkinson for much helpful advice, and to Professor Bradford Hill for help with the statistics.

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THE EARLY DIAGNOSIS OF PHEOCHROMOCYTOMA

BY

LESLIE COLE

From Addenbrook's Hospital, Cambridge

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It is now well known that tumours of the adrenal medulla are a cause of paroxysmal hypertension. It is less generally recognized that these attacks may only occur late or not at all. When this is so, if the risk of surgical treatment is to be reduced to a minimum, diagnosis should be made in the early stages when paroxysmal symptoms are absent and hypertension, if present, closely resembles the benign or malignant form. The first paroxysm may be the last because after it has occurred the patient may be too ill for operation. This paper describes the clinical features of such a patient from the early stages and serves as a basis for discussion of some of the difficulties of diagnosis.

Patients with pheochromocytoma may present in various ways.

(1) With recurrent attacks of paroxysmal hypertension and vasomotor instability, with or without sustained hypertension between attacks.

(2) Without paroxysms with sustained hypertension resembling benign or malignant hypertension.

(3) In extremis, from some cardiovascular accident when previous symptoms have not been severe enough to lead them to consult a doctor.

(4) Simulating Addison's disease from local pressure on the adrenal cortex (Mackeith, 1944).

The classical picture of the adrenal sympathetic syndrome is too well known to need description here. It is characterized by periodic attacks of paroxysmal hypertension with palpitation, anxiety, shakiness, headache, vomiting and vasomotor phenomena. Transient glycosuria may also be present. The similarity of this picture to that produced by the injection of a large dose of adrenalin is evident.

It is less generally known that pheochromocytoma may produce a picture without paroxysms, closely resembling benign or malignant hypertension, but this had been pointed out by many writers (Binger and Craig, 1938; Thorn, Hindle, and Sandmeyer, 1944; Palmer and Castleman, 1938; McCullagh and Engel, 1942; and Mackeith, 1944). That persistent hypertension is a good deal commoner than has been realized, is suggested by Green (1946) who in a recent review of 51 cases of pheochromocytoma found that only 14 showed intermittent hypertension, while 37 had chronic hypertension. Smithwick's (1946) series of 1000 hypertensive patients subjected to lumbodorsal sympathectomy showed an incidence of pheochromocytoma of 0·05 per cent. There is thus considerable evidence to show that sustained hypertension of the benign or malignant type may be due to pheochromocytoma, and it is clear that if the diagnosis is to be made earlier and more frequently, it must be considered as a possible cause in every case until it has been excluded. Soffer (1946) has pointed out that success depends first and foremost on the index of suspicion of the physician. Put more simply, he must think of the possibility in every case of hypertension.

Cases that are first seen in extremis after some cardiovascular accident (Hick, 1933) bear evidence to the fact that paroxysms of hypertension are dangerous and may be fatal and that diagnosis should, if possible, be made before they occur. The case described in this paper is an example of this.

Case Report

A married woman, aged 35, who had been previously healthy was admitted to Addenbrooke's Hospital in October 1946 under Dr. J. R. C. Canney for a severe ante-partem hæmorrhage. Her pregnancy had been uneventful up to this time and her blood pressure normal throughout.

Previously she had always been healthy and active, leading an energetic life as a farmer's wife. She had three children alive and well, aged 8, 5, and 3, and her previous confinements had been without incident. Her husband was healthy and the family history did not reveal any tendency to raised blood pressure, or heart, kidney, or other relevant disease.

On admission she was very anæmic and shocked but no other abnormalities were found, and after a transfusion a stillborn child of 30 weeks was delivered by Cæsarean section. A few days later she developed a slight thrombosis in the left leg but she was discharged apparently well on October 29th, fifteen days after her hæmorrhage.

On November 2nd, in the evening, while she was sitting up in bed, she suddenly developed frontal headache and this persisted. I saw her for the first time on November 5th. She was then complaining of dull continuous headache, frontal and mainly on the right side but spreading over to the left at times. It was worse in the early morning and was accentuated by movement. On examination, there was slight œdema of the left ankle, but there were no other abnormalities. Blood pressure, 130/90; pulse rate, 84; and fundi normal.

During the next four months her general condition improved and she was moderately active, but her headaches continued to trouble her until February 1947 when they cleared up. She remained practically free from symptoms until April, when they returned and continued as before. In July, because they were rather worse, she was readmitted to hospital for investigation.

The headaches were still frontal, sometimes on one side, sometimes on the other. They were worse in the early morning, passed off about noon, and often came back in the evening. They were made worse by effort or movement but nothing else seemed to affect them. She said that at times she used to become very shaky, especially if anything worried her, and attributed this to the shock of the operation (for she had never been ill before) and the fact that she had had a good deal of worry the previous summer. She had no other symptoms.

On examination, her blood pressure was 180/120–130, in both arms. This was taken on many occasions at different times of the day and in different postures and hardly varied. Slight œdema of the left leg was still present. Her urine occasionally contained a trace of albumen, but this was not constant. Clinical examination revealed nothing otherwise; she had no fever and her pulse rate remained between 80 and 90, hardly varying with mild effort. Special investigation only showed a slight *B. coli* bacilluria and a very slight dilatation of the pelvis of the right kidney, which was not considered significant.

The hypertension was thought to be benign and did not seem to be enough to account for her headache, which was the outstanding symptom; and it seemed likely from her general nervousness that there was a considerable functional element present. She was given a course of sulphamezathine for her *B. coli* bacilluria.

During the next three months her headaches persisted except for a three-weeks remission while she was on holiday in August. They maintained the same character and rhythm but grew more severe. In September she began to suffer from short early morning nausea and her appetite began to fail and in October she was readmitted. She said then that her head did not throb but felt at times as if someone were sticking knives into her forehead. She began to retch occasionally. At times she had " peculiar sensations," during which she felt worked up and excited, and on these occasions she looked tremulous and anxious. At times she seemed to be in a state of repressed excitement and shaking like a patient with exophthalmic goitre but without thyrotoxicosis. As vomiting became more frequent her nutrition and general condition began to deteriorate for the first time. During October her blood pressure taken on many occasions varied between 180/120 and 175/115 and her pulse rate was steady between 70 and 80. Clinical examination was otherwise normal and the following special investigations did not help.

Examination of her pelvis, eyes (fundi, visual fields and refraction), ears, nose, and throat, and renal function, were all normal. Blood urea 17 and 28 mg. Urea clearance 90 per cent. Full blood count normal. Sedimentation rate (Westergren) 17 mm. Wassermann and Kahn reactions negative. X-rays of her skull, cervical spine, nasal sinuses, and lungs, all normal. Cardioscopy slight ventricular hypertrophy and slight uncoiling of the aorta. Electrocardiogram, left axis deviation only. The urinary deposit showed epithelial cells only and no albumen or sugar. The cerebrospinal fluid was under pressure (400/350 mm.) but was otherwise normal, and the Wassermann reaction was negative.

On October 31st she was discharged home at her own request pending transfer to a cerebral unit, where her condition remained the same until November 9th. On that afternoon she had some kind of fit, a sudden attack of headache, vomiting, and intense excitement, and her doctor found that her blood pressure rose temporarily to 240/160—a typical paroxysm of hypertension. The same afternoon, her headache dramatically disappeared, she stopped vomiting, and was able to take more food. On the morning of the 10th, her blood pressure had fallen to 170/110 and in the afternoon she was suddenly seized with a very severe pain in the right renal region which did not radiate and only gradually eased. On the 11th the pain was still present and much less severe but her abdomen was slightly distended. Her bowels had not been open since the onset of the pain but she had passed flatus. An acute abdominal condition was suspected and she was readmitted to hospital.

On admission, she was anxious and excited with slight tremor of the hands. Her hands and feet were cold and she sweated profusely at times. Temperature, 101; pulse rate, 110; respiration rate, 20. She looked a little dehydrated. Her headache and vomiting had stopped. The abdomen was slightly distended and there was marked tenderness in the right renal angle and over the right side, but no true rigidity. Vigorous peristalsis was audible and she passed flatus. Rectal examination was normal. The blood pressure was 180/130. The urine contained a heavy cloud of albumen. Microscopically there was no deposit and no other abnormalities were found. Enemas yielded very little result. The next morning her general condition was unchanged. Blood count showed a leucocytosis of 29,000 with 89 per cent polymorphs. During the day her abdomen became more distended and she was seen in consultation with Mr. P. H. R. Ghey. In view of the progressive distension it was thought that she might have general peritonitis with paralytic ileus or subacute obstruction and laparotomy was performed.

No evidence of peritonitis or obstruction was found. The whole of the large and small bowel was distended with gas and the cæcum was enormous. There were a few hard fæcal masses at the hepatic flexure. A round solid tumour about 3 inches in diameter was felt in the region of the left suprarenal which seemed rather fixed. As her general condition was rather poor it was considered inadvisable to attempt to remove this until the ileus had been controlled, so cæcostomy was performed and a de Pezzer catheter inserted.

During the next six days she was given eucortone and glucose saline, plasma or normal saline intravenously at the rate of 4 pints a day, and every effort was made to improve her general condition. This hope was not realized and as it threatened to deteriorate, Mr. Ghey performed a second operation on November 17th. A tumour which subsequently proved to be a typical pheochromocytoma was removed from the site of the left suprarenal gland. Section of the last blood vessels to the tumour was followed by a sudden profound fall in blood pressure. In anticipation of this, an intravenous adrenalin drip (1 : 10,000) which had previously been connected, was turned on at once, but without effect and death took place a few minutes later.

Post-Mortem Report

The following are extracts from the full post-mortem report for which I am indebted to Dr. A. M. Barrett.

Left suprarenal. Thin triangular remnant (sides 3, 2, and 2 cm.) of suprarenal tissue consisting

of two thin layers of yellow cortex without any visible medulla at site of otherwise absent left suprarenal. Considerable enlargement of ligatured and divided left suprarenal blood vessels.

Microscopic sections were normal.

Suprarenal tumour. (Fig. 1.) Ovoid tumour (9·5×7·5×5·7 cm.) enclosed with thin capsule. Wt. 227 g. Near one pole a slightly raised yellow ridge (4×0·3 cm. wide) apparently consisting of suprarenal cortex; small yellow islands are also present here and there elsewhere on the pale grey-brown outer surface. The consistency of the tumour is soft, almost cystic, with dull purplish areas as of hæmorrhage which show through the capsule here and there. The predominant colour of the bulging cut surface is a rich purple-red, but on closer inspection it is seen that there are everywhere close-set purple dots and streaks (about 0·1 cm. diameter) set in a greyish white ground.

FIG. 1.—Photograph of the suprarenal tumour. The measurements were 9·5×7·5×5·7 cm. and the weight 227 g.

Microscopical section. (Fig. 2.) This shows chromaffin tumour of suprarenal medulla, with numerous blood spaces devoid of any lining and also areas of hæmorrhage with necrotic tumour cells.

Right suprarenal. Weight, 9 g. Abundant yellow lipoid, very scanty brown pigment, and normal grey-white medulla in rather large gland. Microscopic sections normal.

Cardiovascular system. Heart weight, 36 g. Moderate hypertrophy of firm, brown-red myocardium of contracted left ventricle (L.V. : R.V., 2·5 : 0·5). No hypertrophy of the rest of the heart. Pale brown ante-mortem thrombosis for the most part only lightly adherent, but in one

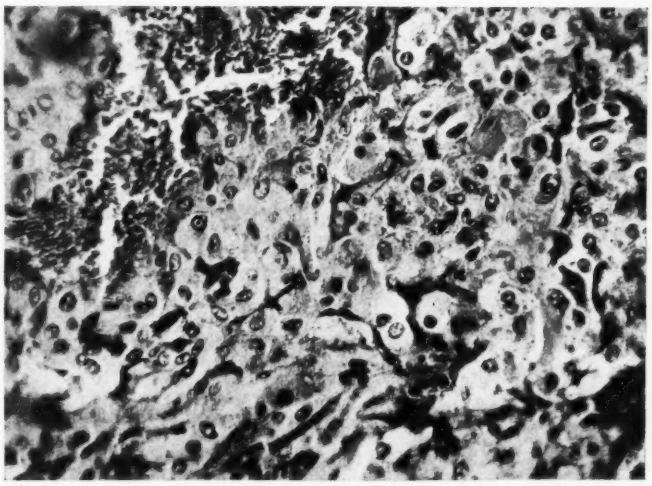

FIG. 2.—Photomicrograph, showing the histological appearances of the tumour.

place apparently merging with the underlying muscle lining the apex of left ventricle. Moderate atheroma without narrowing in the coronary arteries. Slight to moderate atheroma of normal-sized aorta. Thrombosis of right and left posterior tibial veins and of left femoral vein.

On section the mural thrombosis was shown to have formed ante-mortem.

Respiratory system. About a dozen fragments of ante-mortem clot impacted in branches of the pulmonary arteries in both lungs. The emboli were about 1 cm. in diameter. Altogether they must have caused considerable reduction in the arterial " bed " of the lungs.

Urogenital system. Many yellow-white areas of infarction in the right kidney apparently involving altogether about half its substance. On the outer surface the infarcted areas were neither raised nor sunken. Scanty fibrinous exudate on the outside of the capsule of the right kidney. This embolus satisfactorily accounted for the largest area of infarction, but there were many other smaller areas. Slight dilatation of right renal pelvis. No infarction of well developed left kidney.

On section, infarction with fibrinoid degeneration of afferent glomerular arterioles and other abnormalities of glomerular tufts which are probably related to it.

Special investigations. The chromaffin reaction (Schmorl) was positive.

The test for adrenalin by Craner's method was very suggestive of the presence of much adrenalin.

The test by Masson's method showed that argentaffin cells appeared to be present.

Discussion

When paroxysmal hypertension is absent a tentative diagnosis of pheochromocytoma would appear to depend more on careful consideration of the symptoms found in association with hypertension than on the physical signs, which are not distinctive unless the tumour is palpable.

The syndrome presented by this patient was quite different from any I had seen before, and during the three months before her attack of paroxysmal hypertension presented a clinical picture that once seen could not be forgotten or pass unrecognized again. It is, therefore, worth studying her symptoms and signs in detail.

The unusual clinical features in the early stages appeared to be as follows: the sudden onset of headache preceding the rise in blood pressure, the periodicity of the headache in the early morning and evening, the " peculiar sensations " in the upper abdomen with sinking feelings, turmoil, and excitement, and the slow but steady increase in the intensity of the symptoms without any corresponding rise in blood pressure.

In the later stages the unusual features were the severity of the headache, out of all proportion to the blood pressure, and its character—" like knives being driven into the head "—and the attacks of sweating and cold hands and feet.

It is also worth noting that this syndrome developed in a patient who had been particularly well balanced mentally and physically in the past, and had never previously had a headache in her life, and was without any obvious hereditary or environmental causes for her symptoms.

Further special investigations that might have been done to establish the diagnosis earlier may conveniently be considered under the three following headings.

(1) *Tests that suggest hypersecretion of adrenalin.* Attempts to demonstrate the presence of a pressor substance in the blood have only occasionally been successful, are difficult to perform, and cannot be relied on. Beer, King, and Prinzmetal (1937), by perfusing a denervated rabbit's ear with blood obtained from a patient during an induced paroxysm, were able to demonstrate the presence of such an active principle. Because of the great practical difficulties that attend this method, it cannot often be applied clinically.

Paroxysms can sometimes be induced deliberately, but this is not devoid of risk. Massage or manipulation of the tumour by change of posture sometimes bring on an attack and indirectly give a clue to its site. Starvation for from 12 to 24 hours may induce one (Soffer, 1946), or the injection of adrenalin (Mackeith, 1944). Since the greatest difficulties in diagnosis occur in patients in whom

the existence and site of the tumour are not known, the injection of adrenalin is the easiest, but because of its risk is perhaps better avoided.

Shortly after this patient died, Goldenberg (1947) described a simple test for hypertension caused by excess circulating adrenalin and claimed to have established its value in the diagnosis of pheochromocytoma. Briefly, the test consists in perfusing the patient with benzodioxanes (1164F or 933 F) which given in the appropriate dose are adrenolytic in action and block sympathetic activity. He found that in patients with pheochromocytomas or with hypertension induced by perfusion with adrenalin, blood pressure readings taken over a period of 15 minutes after the injection showed a characteristic fall that was in contrast to the rise obtained in those with malignant or essential hypertension. Smithwick (1948) confirmed the diagnostic value of this test and if further observations confirm Goldenberg's findings, it should be of great benefit in helping to diagnose difficult cases of pheochromocytoma in the early stages. It is clearly easier to localize the tumour when there is strong evidence that it is present than when its existence is still in doubt.

Another test for pheochromocytoma is by intravenous injection of histamine. It is claimed that this is followed immediately by a rise in blood pressure in contrast to the usual fall obtained in normal people. Roth and Kuale (1945) suggest that this test is specific for the condition.

(2) *Localization of the tumour.* This may be easy or it may be very difficult. It may be palpable or only observable by exploration and may be found by accident in the course of operation for lumbo-dorsal sympathectomy in hypertension or as in the present case for some complication. It is noteworthy that in the patient described here, while all the signs and symptoms pointed to the right side, the pheochromocytoma was on the left. It should also be remembered that bilateral tumours may occur (Reid and Salm, 1949). If the tumour is not palpable, radiological investigation of the kidneys is the procedure most likely to yield definite evidence. Howard and Barker (1937) estimated that an intravenous pyelogram would have suggested the presence of the tumour in 11 of these 18 cases. If this measure fails a retrogade pyelogram or even perirenal insufflations with oxygen have proved invaluable (Soffer, 1946). It is important, too, to remember that the position of these tumours in the abdomen is very varied. They may also be located in the neck and even in the chest, but do not appear to be active in these situations (Phillips, 1940). Diagnostic procedures should be as innocuous as possible because these patients stand manipulation badly. This makes it all the more desirable that the tumour should be located early and accurately.

(3) *Other investigations.* The basal metabolic rate perhaps comes next in order of importance for this is often above 20 per cent (Binger, 1938, and McCullagh, 1942) and indeed the differential diagnosis from hyperthyroidism may be very difficult and has often led to confusion. This is not surprising, for the clinical resemblance between excessive secretion of adrenalin, chronic anxiety, and hyperthyroidism may be very close. Mistakes will be less likely to occur if this resemblance is remembered in typical cases of hyperthyroidism coupled with the fact that the B.M.R. is often raised in pheochromocytoma.

Other investigations are useful chiefly for excluding intercurrent disease and for demonstrating changes that occur in hypertension from any cause but are not specific for pheochromocytoma. Thus cardiographic studies may show changes associated with hypertension; cardioscopy, general cardiac enlargement, and left ventricular hypertrophy; and renal function tests, a greater or lesser degree of impairment but nothing diagnostic.

Glycosuria and a raised blood sugar have been found occasionally and although the association of these with excessive secretion of adrenalin is clear, they do not occur frequently enough to be of much value in diagnosis. Pheochromocytoma has also been found with frank diabetes mellitus (McCullagh, 1942). Retinal changes do not differ from those found in benign or malignant hypertension. Blood counts do not show any significant change. The high pressure in the cerebrospinal fluid found in this patient has also been recorded in another (Palmer, 1938) but might well occur in hypertension from any other cause. If for any reason lumbar puncture is considered advisable, the risk of its provoking a paroxysm must be remembered, and the blood pressure and general condition carefully measured both before and after.

Summary

The symptoms in a patient with sustained hypertension due to pheochromocytoma are described in detail. The diagnosis is discussed and the importance of early diagnosis is emphasized.

The author wishes to thank Dr. A. M. Barrett for the post-mortem report and Mr. H. P. Hudson for the photograph and photomicrograph.

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CYCLOPROPANE ANÆSTHESIA AND VENTRICULAR ARRHYTHMIAS

BY

MICHAEL JOHNSTONE

From Townley's Hospital, Bolton, Lancashire

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Much attention has recently been focused on the ætiology and control of the cardiac arrhythmias associated with cyclopropane anæsthesia. This gas possesses several advantages over the other anæsthetics in general use, being non-irritant, giving rapid induction, excellent relaxation, quiet respiration and speedy recovery of consciousness. The high incidence of cardiac arrhythmias during cyclopropane anæsthesia remains a very serious disadvantage, particularly for patients with myocardial disease.

The arrhythmias are mainly of ventricular origin and include occasional ventricular extrasystoles, bigeminal rhythms, ventricular tachycardia, and ventricular fibrillation. These irregularities cause considerable impairment of cardiac efficiency and Wright (1940) has stated that ventricular tachycardia diminishes the cardiac output by more than half. Levy (1911) has noted that ventricular tachycardia often precedes ventricular fibrillation.

The bulk of the evidence from animal experiments suggests that the cardiac irregularities are of reflex origin, associated with sympathetic stimulation, and are not due to direct action on the myocardium or its conducting mechanism. Meek, Hathaway and Orth (1937) found that cyclopropane, like chloroform, caused sensitization of the heart to the action of adrenalin, the injection of which caused ventricular fibrillation.

Brow, Beattie and Long (1930), working with chloroform, found in the region of the hypothalamus a centre, the stimulation of which caused ventricular extrasystoles. Interruption of the sympathetic pathway between the central nervous system and the heart prevented the occurrence of these ectopic beats. Stimulation of the peripheral end of the cut vagus abolished the extrasystoles. Allen *et al.* (1940), made similar observations during cyclopropane anæsthesia. Stutzman and Pettinga (1949) found that partial abdominal evisceration, partial abdominal denervation, or bilateral adrenalectomy abolished the ventricular arrhythmias associated with cyclopropane anæsthesia in cats.

Various methods have been suggested to prevent and abolish these arrhythmias during surgical anæsthesia in man, but none of them has been entirely satisfactory. Lundy (1942) advocates the addition of ether to the cyclopropane–oxygen mixture. Robbins and Baxter (1939) advised barbiturate premedication. Guedel (1942) suggested that there was an "arrhythmic phase" during cyclopropane anæsthesia, above or below which arrhythmias did not appear. He therefore advised high concentration of cyclopropane. The position regarding the intravenous administration of procaine is controversial. Burstein (1949) abolished cardiac irregularities during anæsthesia by this method. Long *et al.* (1949), have induced fatal ventricular arrhythmias in dogs under barbiturate anæsthesia by administering procaine intravenously.

It would appear that cyclopropane anæsthesia brings about an increase in sympathetic tone, which, in turn, gives rise to hyper-irritability of the ectopic centres in the ventricles. Brow *et al.* (1930), have pointed out that stimulation of the peripheral end of the cut vagus inhibits these centres and abolishes ventricular extrasystoles. The significance of this observation will be discussed later.

It is generally accepted that either mild degrees of oxygen lack or CO_2 accumulation in the tissues may cause sympathetic stimulation. The object of the present investigation is to ascertain the influence of these two conditions on cardiac rhythm during cyclopropane anæsthesia in man. There is no doubt that both conditions occur, because cyclopropane, in therapeutic doses, causes a progressive depression of respiration to the point of complete respiratory arrest. This depression is still further augmented by several of the drugs used in conjunction with cyclopropane anæsthesia, such as morphia, thiopentone and curare.

Ninety patients have been investigated. The operations included herniorrhaphies, colpoperineorrhaphies, and laparotomies for cholecystectomy, gastrectomy, appendicectomy, and hysterectomy. All patients were in the supine position and cases in which there was mechanical interference with respiratory activity, as in thoracotomy or the Trendelenberg position, have been excluded. Each patient was given atropine 1/100 or 1/50 of a grain before operation, but no pre-operative sedatives were given. Anæsthesia was induced either with pentothal 0·5 g. or with kemithal 1 g. injected intravenously and only a simple oro-pharyngeal airway was used in each instance. Only those patients in whom there was a perfectly free respiratory exchange, with no evidence of laryngeal or bronchial spasm, have been included. No intravenous therapy was administered either before or during the operation. The Coxeter-Mushin closed circuit anæsthetic machine was used. This apparatus allows of easy manual assistance to respiration and the absorber can be turned off and on without any interference with the gaseous contents of the circuit.

The Cambridge portable electrocardiograph was used and the galvanometer string was under constant observation from before induction till five minutes after the removal of the mask at the end of the operation. Tracings were taken whenever a change in rhythm was noticed or at intervals during the operation. About 700 tracings were obtained and all the changes of rhythm quoted below have been confirmed by electrocardiogram. In order to establish the closest possible relation between the clinical details of anæsthesia and the changes in cardiac rhythm the writer took responsibility for the administration of the anæsthetics as well as for the observation of the galvanometer string.

Methods of Observation

The 90 patients investigated during cyclopropane anæsthesia fell into four groups according to the existence or otherwise of hypoxia, CO_2 accumulation, and hyperventilation. The conditions studied in each group were as follows:

(1) effects of hypoxia,
(2) effects of hypoxia and CO_2 accumulation,
(3) effects of hyperventilation and CO_2 accumulation, and
(4) effects of hyperventilation and deep anæsthesia.

Effects of hypoxia. The group consisted of twenty-five patients undergoing major intra-abdominal operations. In each case, respiration was assisted from the moment that consciousness was lost and the CO_2 absorber was turned on throughout the operation. When anæsthesia was established with cyclopropane, hypoxia was allowed to occur by failing to assist the respiration and allowing only spontaneous depressed respirations to occur for a period of five to fifteen minutes. During the period of hypoxia, ventricular arrhythmias occurred in every case; ventricular tachycardia in three and bigeminal rhythm in the remainder. The resumption of assisted respiration was followed by the return of regular sinus rhythm in each case in from two to three minutes (Fig. 1). The addition of ether for a few seconds caused the immediate disappearance of the ventricular ectopic beats in six of the patients. No extrasystoles were present during the periods of assisted respiration.

Effects of hypoxia and CO_2 accumulation. The group consisted of fifteen patients undergoing laparotomies. The procedure was similar to that in the first section, with the exception that the absorber was excluded from the circuit when assisted respiration was resumed after the period of hypoxia. During the hypoxic periods, ventricular extrasystoles occurred in each patient. When

assisted respiration was resumed, without the absorber, the extrasystoles gradually increased in frequency till, after an average period of fifteen minutes, ventricular tachycardia ensued in twelve of the patients. In each case the ventricular arrhythmias disappeared in from three to six minutes after the insertion of the absorber, respiration being assisted all the time (Fig. 2).

Hyper-ventilation and CO_2 accumulation. In this series, twenty-five patients were anæsthetized with cyclopropane and anæsthesia was maintained at as light a level as possible so as to cause the

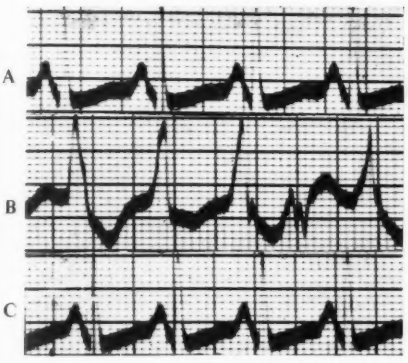

FIG. 1.—All lead II.

(A) After thirty minutes of cyclopropane anæsthesia, with assisted respiration and CO_2 absorption.
(B) Spontaneous, depressed respiration for the previous ten minutes, with CO_2 absorption.
(C) Assisted respiration resumed three minutes previously.

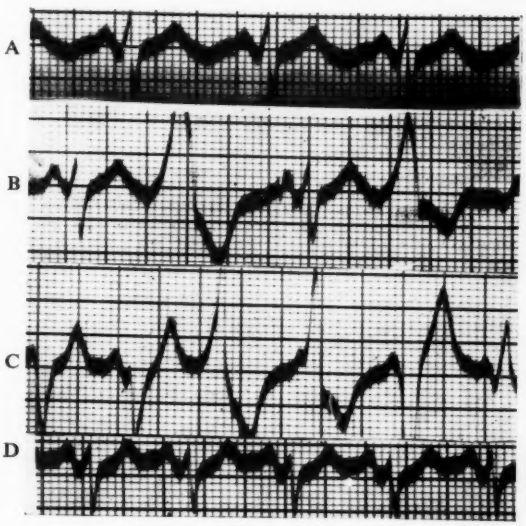

FIG. 2.—All lead II.

(A) After eleven minutes of cyclopropane anæsthesia, with assisted respiration and CO_2 absorption.
(B) Spontaneous, depressed respiration for the previous five minutes, with CO_2 absorption.
(C) Absorber turned off and assisted respiration resumed twenty minutes previously.
(D) Absorber inserted seven minutes previously.

minimal amount of respiratory depression. The operations were mainly herniorrhaphies, mastectomies and other operations not requiring deep anæsthesia. In each case, spontaneous respiration was present throughout the period of anæsthesia. CO_2 was allowed to accumulate in the circuit by failing to insert the absorber for periods ranging from ten to thirty minutes. Ventricular arrhythmias appeared in every case, including ventricular tachycardia in six of them during the period of CO_2 accumulation with hyper-ventilation and, in each case, disappeared within three or four minutes after the insertion of the absorber (Fig. 3). In five cases, the ventricular ectopic beats were abolished immediately by turning on ether for a few seconds.

Hyperventilation in deep anæsthesia. Twenty-five patients undergoing major intra-abdominal operations under deep cyclopropane anæsthesia included many patients with severe myocardial disease, e.g. coronary insufficiency, myocardial infarcts, auricular fibrillation of rheumatic or degenerative origin, five cases of bundle branch block, and a few with frequent ventricular extrasystoles. In each case, the respirations were assisted from the moment that consciousness was lost till the return of brisk reflexes during the recovery period. During anæsthesia, there was no

evidence of ventricular arrhythmias in any of the patients, including those in whom ventricular extrasystoles were present prior to induction. The cases with auricular fibrillation were uninfluenced, apart from slight increases in the ventricular rate. The general conditions of these patients remained satisfactory throughout the operations and some of them seemed in better condition and appearance during anæsthesia than prior to induction.

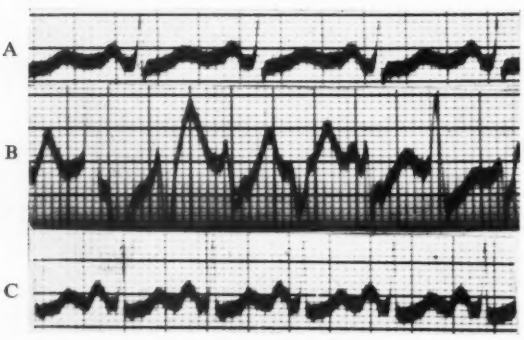

FIG. 3.—All lead II.
(A) Before induction of anæsthesia.
(B) After twelve minutes of cyclopropane anæsthesia, with CO_2 accumulation. Hyper-ventilating.
(C) Absorber inserted four minutes previously.

DISCUSSION

These observations indicate carbon dioxide accumulation as the factor that precipitates ventricular arrhythmias during cyclopropane anæsthesia. This accumulation is due to respiratory depression and does not appear to be related to inhibition of the carbonic anhydrase as the CO_2 can be readily eliminated by assisting the respiratory excursion. The mode of action of CO_2 is obscure but, judging from the work of Stutzman and Pettinga (1949) and others, it probably has a sympathomimetic effect which gives rise to liberation of adrenalin and the appearance of cardiac irregularities. This adrenergic effect may account for the rise in blood pressure, hyperglycæmia, excessive capillary oozing, and various other metabolic changes that occur during general anæsthesia.

Oxygen lack does not appear to influence the arrhythmias in any way, nor does induction of anæsthesia with a short acting barbiturate prevent their occurrence. This type of induction, however, eliminates the sympathetic stimulation associated with the fright and resistance to induction by inhalation and therefore postpones the onset of the arrhythmias. Several workers have noted that ventricular arrhythmias are more common during the induction phases of anæsthesia with cyclopropane, chloroform, and ethyl chloride (Hill, 1932; Kurtz *et al.*, 1936).

There does not appear to be any appreciable difference between the incidence of ventricular extrasystoles during anæsthesia in patients with normal cardiovascular systems and in those with cardiovascular disease. The cardiac irregularities seem to occur more readily in young healthy hearts, particularly in women, and disappear more rapidly when the respiratory exchange is amplified. The longer the period of CO_2 accumulation, the more difficult it is to abolish the irregularities by assisting the respirations, but I have not failed to abolish them in any case in which they have been allowed to occur.

Judging from the results in the fourth section, and in numerous unrecorded cases, the occurrence of ventricular arrhythmias during cyclopropane anæsthesia can be prevented by assisting respiration during the administration of cyclopropane. The assistance ensures an adequate intake of oxygen and output of CO_2. It has already been demonstrated by Dripps (1947) that there is a marked rise in CO_2 tension during cyclopropane anæsthesia and that, at the conclusion of the anæsthetic, this accumulated CO_2 is very rapidly eliminated. This sudden drop in CO_2 tension is associated with a profound fall in blood pressure and collapse of the patient. The condition is referred to as " cyclopropane shock." It has been my experience that this form of post-operative collapse can be completely eliminated by assisting the respirations during the period of anæsthesia.

It has already been demonstrated that the inhalation of an irritant vapour causes reflex vagal inhibition of the heart by stimulation of vagal receptors in the air passages. This is known as the pulmocardiac reflex and its activity is unimpaired by surgical anæsthesia with any of the usual

agents. Stimulation of this reflex causes inhibition of the S-A and A-V nodes, and pacemaker shift to the A-V node in atropinized subjects (Johnstone, 1948). It also inhibits the ectopic centres in the ventricles and this explains the immediate abolition of ventricular arrhythmias during cyclopropane anæsthesia by the addition of ether to the inhaled mixture. This addition renders the inhaled gases more irritant. Stimulation of this reflex also occurs if high and irritant concentrations of cyclopropane are administered, causing inhibition of the ventricular centres. These centres escape when the anæsthetic is removed, with the result that ventricular extrasystoles may reappear during the recovery period (Thienes *et al.*, 1941).

In order to control successfully cyclopropane arrhythmias, the various factors that lead to CO_2 accumulation must be avoided. The most important of these is respiratory depression. This is overcome by avoiding pre-operative sedation, and assisting respiration during the period of anæsthesia, particularly when curare has been administered or when respiratory movement is embarrassed by the posture of the patient on the operating table, as in the Trendelenberg positions. Perfectly free airways must be maintained and obstruction by the tongue, excessive mucus formation, or laryngeal or bronchial spasm must be avoided. The latter can be overcome by cocainization of the air passages. The anæsthetic apparatus should also receive attention, especially the uni-directional valves which tend to become impaired by the condensation of moisture in the circuit. Soda-lime should be renewed at reasonable intervals. Soda-lime that is sufficiently active to prevent hyperventilation may not be active enough to prevent the appearance of extrasystoles.

Direct observation of the galvanometer is the only method by which ventricular arrhythmias can be recognized with certainty. Pulse palpation is often misleading as relatively slow ventricular rhythms are indistinguishable from rapid sinus rhythms and bigeminal rhythms are often almost regular, the only noticeable change being a slight decrease in the volume of alternate beats. The extrasystole often fails to reach the peripheral arteries with the result that palpation reveals an apparent bradycardia.

Summary

The effects of CO_2 accumulation, oxygen lack, and assisted respiration have been investigated in ninety patients during cyclopropane anæsthesia.

It has been observed that CO_2 accumulation precipitates ventricular arrhythmias during cyclopropane anæsthesia. The efficient elimination of CO_2 by assisting the respirations prevents the occurrence of ventricular arrhythmias and also abolishes them when present.

Ventricular arrhythmias may occur in any patient during cyclopropane anæsthesia provided the CO_2 tension in the circuit is allowed to become sufficiently high.

The causes of CO_2 accumulation have been enumerated and the influence of this on the condition known as " cyclopropane shock " has been discussed.

This paper is partly an extract from an M.D. thesis. I wish to express my gratitude to Mr. E. S. Gawne, F.R.C.S., for granting me permission to do the work, and to Professor Crighton Bramwell for his assistance in the preparation of the paper.

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ANGINA PECTORIS AND THYROTOXICOSIS

BY

WALTER SOMERVILLE * AND S. A. LEVINE

From the Medical Clinic of the Peter Bent Brigham Hospital and the Department of Medicine, Harvard Medical School, Boston, Massachusetts

Received September 10, 1949

The effects of thyrotoxicosis on the cardiovascular system are well recognized and some are very prominent. Symptoms ascribable to the overaction of the heart such as dyspnœa, palpitation, tachycardia, irregularity of the heart, dizziness, and præcordial pain have been encountered in as many as 80 per cent of a series of 148 cases of thyrotoxicosis (Burnett and Durbin, 1932). The pathological changes in the heart occasionally associated with thyrotoxicosis have been described by Goodpasture (1921) who believed that infection might play a part in their production, and by Goodall and Rogers (1927), who concluded that the perivascular infiltration, fatty degeneration, and fibrosis which they encountered were specific effects of thyroid secretion. This view has been challenged by many authors (Rake and McEachern, 1932; Menne *et al.*, 1932; Means, 1948), and the view that they represent non-specific reactions to prolonged overactivity of the heart is widespread today (White, 1944; Levine, 1945; Means, 1948). When heart disease of rheumatic, hypertensive, arteriosclerotic, or other ætiology is present in a person who develops thyrotoxicosis, the diagnosis of the latter may be missed by reason of the pre-eminence of the signs and symptoms of the underlying heart disease. On the other hand, thyrotoxic effects on the cardiovascular system may resemble closely those of organic heart disease especially mitral stenosis and the correct diagnosis may be overlooked (Levine and Sturgis, 1924; Levine and Walker, 1929; Levine, 1930; Rosenblum and Levine, 1933).

When coronary arteriosclerosis is present with thyrotoxicosis, angina pectoris may be brought to light, or if this symptom is already present, it may be aggravated by the increased demands on the heart. The frequency and severity of the angina may occasionally so dominate the clinical picture that the thyrotoxic element may pass undetected. The association of these two conditions is said to be uncommon, Means (1948) encountering only one thyrotoxic patient in whom angina pectoris was the presenting symptom. White (1944) states that angina pectoris rarely accompanies thyrotoxicosis, and then only in older persons with underlying coronary artery disease. Only a few reports on the subject have appeared. In a follow-up study of 69 thyrocardiacs on whom subtotal thyroidectomy had been performed, Rosenblum and Levine (1933) reported 9 with angina pectoris; in the course of observation periods ranging from four months to four years, the attacks in every instance either completely disappeared or were greatly improved. Haines and Kepler (1930) described 33 patients with angina pectoris and thyrotoxicosis, 28 of whom were treated by subtotal thyroidectomy; only two of the treated patients failed to improve in their anginal symptoms over periods of four months to seven years after operation. Lev and Hamburger (1932) observed 5 patients with the same combination, 5 of them for two to five years; no further attacks of angina occurred in any of them after subtotal thyroidectomy. Other authors have experienced similar favourable results (Duchosal and Henny, 1941; Fischer, 1941).

The present report deals with 24 patients with angina pectoris and thyrotoxicosis, and their main features are summarized in Table I. Seven of them were included in a previous communi-

* Travelling Fellow in Medicine, British Postgraduate Medical Federation, from the Institute of Cardiology, London.

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TABLE I

SUMMARY OF CLINICAL DATA: ANGINA PECTORIS AND THYROTOXICOSIS (24 PATIENTS)

Case No.	Sex and Age	Angina Pectoris [1]					Duration of thyrotoxicosis		Before treatment	After treatment	Treatment	Observ. period (years)	Result
		Hist. of myocard. infarct.	Years since onset		Before treatment of thyrotox.	After treatment of thyrotox.							
1	F. 63	—	3	Severity Pain at rest.	++ Yes	+ No	4 yrs.	B.M.R. B.P. Heart rate Heart size [2]	+43 135/80 80 (AF) ++	−8 170/110 — ++	Sub-total thyroid-ectomy.	2½	Relieved for 8 mo. Developed congestive failure. Died 2½ years after operation.
2	M. 63	—	5	Severity Pain at rest.	+++ Yes	0 No	1 yr.	B.M.R. B.P. Heart rate Heart size	+41 145/80 100 +	+4 — 80 +	Sub-total thyroid-ectomy.	12	Free of A.P. for 10 yrs. Then pain returned. Died suddenly 2 yrs. later.
3	M. 52	Yes	7	Severity Pain at rest.	++ Yes	0 No	Uncertain	B.M.R. B.P. Heart rate Heart size	+60 105/65	0 130/90	Sub-total thyroid-ectomy.	11	Free of A.P. for 10 yrs. Died from congest. failure.
4	M. 62	—	2	Severity Pain at rest.	++ Yes	+ No	4 mo.	B.M.R. B.P. Heart rate Heart size	+32 160/100 75 (AF) +	— — — +	Sub-total thyroid-ectomy.	12	Free of A.P. for 12 yrs. Died from cerebro-vascular accident.
5	M. 31	—	4 mo.	Severity Pain at rest.	++ Yes	0 No	Uncertain	B.M.R. B.P. Heart rate Heart size	+27 140/80 140 +	−23 170/115 72 +	Sub-total thyroid-ectomy.	17	Free of A.P. for 17 yrs. Alive and well.
6	M. 62	—	4	Severity Pain at rest.	+ No	0 No	6 mo.	B.M.R. B.P. Heart rate Heart size	+25 180/110 140 N	−13 — 70 N	Sub-total thyroid-ectomy.	17½	Free of A.P. for 17 yrs. Alive and well.
7	M. 52	Twice	6 mo.	Severity Pain at rest.	+++ Yes	0 No	Uncertain	B.M.R. B.P. Heart rate Heart size	+35 120/75 85 N	+7 120/75 60 N	Sub-total thyroid-ectomy.	11	Free of A.P. for 11 yrs. Then returned.
8	F. 42	—	4 mo.	Severity Pain at rest.	++ Yes	+ No	4 mo.	B.M.R. B.P. Heart rate Heart size	+81 145/85 110 N	−12 145/85 100 N	Sub-total thyroid-ectomy.	8	A.P. only on unusual effort.

				Heart size	N				N				
9	M. 65	—	2 mo.	Severity Pain at rest.	++ Yes	0 No	1½ yrs.	B.M.R. B.P. Heart rate Heart size	+59 130/80 126 N	−3 135/90 76 N	Sub-total thyroid-ectomy.	1	Free of A.P. for 1 yr. Alive and well.
10	F. 50	—	1	Severity Pain at rest.	++ Yes	0 No	2 yrs.	B.M.R. B.P. Heart rate Heart size	+6 180/110 72 N	−20 140/95 66 N	Sub-total thyroid-ectomy.	1	Free of A.P. for 1 yr. Alive and well.
11	F. 41	—	2 mo.	Severity Pain at rest.	+++ Yes	0 No	1 yr.	B.M.R. B.P. Heart rate Heart size	+12 130/80 100 N	+3 160/90 72 N	Sub-total thyroid-ectomy.	11½	Free of A.P. for 10 yrs. Pain returned. Died from myocardial infarction.
12	M. 66	Yes	2	Severity Pain at rest.	+++ Yes	0 No	1 yr.	B.M.R. B.P. Heart rate Heart size	+50 140/90 100 +	−8 175/105 69 N	Sub-total thyroid-ectomy	7½	Free of A.P. for 4 yrs. Returned for 4 yrs. Died suddenly.
13	M. 53	—	10 mo.	Severity Pain at rest.	++ No	++ No	8 mo.	B.M.R. B.P. Heart rate Heart size	+21 210/135	−4 180/135	Sub-total thyroid-ectomy.	1½	A.P. improved for few months. Then returned in spite of controlled thyrotoxicosis. Died 18 mo. postoperative.
14	M. 61	Yes	1	Severity Pain at rest.	+ No	Died	6 mo.	B.M.R. B.P. Heart rate Heart size	+68 160/90 100 ++	Died	Sub-total thyroid-ectomy.	1 mo.	Died day after sub-total thyroidectomy. Autopsy showed recent occlusion.
15	M. 51	—	2½	Severity Pain at rest.	+++ Yes	+ No	1 yr.	B.M.R. B.P. Heart rate Heart size	+26 140/90 90 N	+5 135/80 80 N	Sub-total thyroid-ectomy.	5	Free of A.P. for 5 yrs. Alive and well.
16	M. 63	—	1½ mo.	Severity Pain at rest.	+++ Yes	0 No	Uncertain	B.M.R. B.P. Heart rate Heart size	+61 160/90 118 +	−10 190/95 60 N	Propyl-thiouracil	2	Free of A.P. for 2 yrs. Alive and well.
17	M. 55	—	2	Severity Pain at rest.	+++ No	0 No	2 yrs.	B.M.R. B.P. Heart rate Heart size	+36 140/75	+2 160/85	Propyl-thiouracil	15 mo.	Free of A.P. for 1¼ yrs. Alive and well.
18	M. 50	—	2	Severity Pain at rest.	+++ Yes	+ No	1½ mo.	B.M.R. B.P. Heart rate Heart size	+49 120/80 76 N	+13 135/80 80 N	Thiouracil	5	A.P. only on unusual effort.

TABLE I—*continued*

SUMMARY OF CLINICAL DATA: ANGINA PECTORIS AND THYROTOXICOSIS (24 PATIENTS)—*continued*

Case No.	Sex and Age	Angina Pectoris [1]					Duration of thyrotoxicosis		Before Treatment	After Treatment	Treatment	Observ. period (years)	Result
		Hist. of myocard. infarct.	Years since onset		Before treatment of thyrotox.	After treatment of thyrotox.							
19	M. 55	—	8	Severity Pain at rest.	+++ Yes	0 No	6 yrs.	B.M.R. B.P. Heart rate Heart size	+80 140/70 100 N	−14 120/70 60 N	Radio-active Iodine and thioura-cil.	7	A.P. improved. Pain only on unusual effort.
20	F. 49	Yes	2	Severity Pain at rest.	++ Yes	++ Yes	1 yr.	B.M.R. B.P. Heart rate Heart size	+25 150/95 120 ++	+25 220/110 100 ++	Propyl-thioura-cil.	3 mo.	Thyrotoxicosis poorly controlled. Continued to have A.P. on effort.
21	M. 47	—	1 mo.	Severity Pain at rest.	++ Yes	— —	Uncertain	B.M.R. B.P. Heart rate Heart size	+39 150/90 100 N	— — —	None	2 weeks	Died suddenly 2 weeks after diagnosis.
22	M. 46	—	10 mo.	Severity Pain at rest	+++ Yes	— —	Uncertain	B.M.R. B.P. Heart rate Heart size	+36 110/85 100 N	— — — —	None	2 weeks	Died suddenly after severe chest pain 2 weeks after first consultation.
23	F. 68	—	2½	Severity Pain at rest.	+ No	— —	6 mo.	B.M.R. B.P. Heart rate Heart size	+68 160/90 100 ++	— — — —	None	11 mo.	Continued to have A.P. until death.
24	M. 56	—	2	Severity Pain at rest.	+ No	— —	Uncertain	B.M.R. B.P. Heart rate Heart size	+25 120/90 130 N	— — — —	None	8	Continued to have A.P. for 8 yrs. Died in sleep.

[1] Angina was graded as mild (+), moderately severe (++), or severe (+++) according to provocative factors and frequency of attacks, occurrence of pain at rest and response to nitroglycerine.

[2] Heart size was graded as normal (N), slightly enlarged (+), moderately enlarged (++), or markedly enlarged (+++).

cation (Rosenblum and Levine, 1933). We are indebted to Dr. Paul D. White for allowing us to include Cases 11, 12 and 24 from his private files, and to Dr. E. F. Bland for Cases 14 and 19 from the files of the Massachusetts General Hospital. The remainder were observed at the Peter Bent Brigham Hospital or in the private practice of one of us (S. A. L.).

Symptoms and Signs

The symptoms and signs of thyrotoxicosis most frequently encountered in this series are detailed in Table II. For comparison, the occurrence of these symptoms in 150 unselected cases of thyrotoxicosis without angina pectoris, drawn from approximately the same part of the United States, is included alongside (Means and Richardson, 1938).

TABLE II

Symptoms of Thyrotoxicosis: Comparison in Patients With and Without Angina Pectoris

Symptom	Thyrotoxicosis with angina pectoris (Present series: 24 cases) (per cent)	Thyrotoxicosis without angina pectoris (Means and Richardson, 1938: 150 cases) (per cent)
Increased sweating	75	78
Tremor	67	98
Nervous instability	50	100
Weight loss	50	84
Tachycardia	42	99
Goitre	38	94
Von Graefe's sign	38	63
Palpitation	25	91
Dyspnœa	25	81
Exophthalmos	17	83
Thyroid bruit	13	81
Increased appetite	13	66
Diarrhœa	13	29
Asthenia	8	81
Möbius' sign	8	35
Pressure symptoms	4	25

The striking difference between the overall incidence of symptoms in the two groups indicates that when angina occurs with thyrotoxicosis, the latter is likely to present itself in a subclinical form, and the clue to its presence may be a few, or even a single, subjective or objective finding. In several instances in the present series, the possibility of thyrotoxicosis was first suggested by prematurely grey hair, salmon coloration of the skin, transient glycosuria, or paroxysmal auricular fibrillation: the masked nature of the thyrotoxicosis may be explained partly by the age and sex distribution of the patients. Means (1948) has noted that the symptoms of thyroid overaction become less pronounced with advancing years, and that, for a given rise in metabolism men tend to have more symptoms than women. Our patients were drawn from the age range in which angina is prevalent, and their average age (54 years) was higher than that of the non-anginal thyrotoxic group in which most cases start between the ages of 15 and 49 (Means, 1948). Women with thyrotoxicosis usually outnumber men six to one (Means, 1948) but our series comprises 18 men and 6 women. Therefore, apart from any effect which the co-existence of angina may have had on the thyrotoxic manifestations, the greater average age and preponderance of men in the series would tend to mask the clinical features of thyrotoxicosis.

The cases are a special group which may be peculiarly biassed. In almost all cases the thyrotoxicosis had been overlooked because the two most obvious manifestations (enlarged thyroid

gland and exophthalmos) were either absent or inconspicuous. Had the more obvious evidence of thyrotoxicosis been present and been detected by the physician who had previously seen these cases, they probably would have been sent directly to a surgeon and not been seen by a cardiologist. This may partly explain the greater scarcity of symptoms of thyrotoxicosis in this group as compared to the ordinary case of thyrotoxicosis.

Sex Distribution

The relative numbers of men and women in this series (18 to 6) follows the expected sex distribution in angina pectoris in which the ratio is usually three or four to one (Eppinger and Levine, 1934; White, Bland and Miskall, 1943). Other authors who have reported on the association of angina pectoris and thyrotoxicosis have not found a predominance of men. Haines and Kepler (1930) described 33 cases, 16 of whom were men and 17 women, while in Lev and Hamburger's series (1932), there were three men and six women. Therefore, it would appear that there is no characteristic sex distribution of angina pectoris associated with thyrotoxicosis.

Effect of Treatment of Thyrotoxicosis on Angina Pectoris

In 20 patients, the thyrotoxicosis was treated by either subtotal thyroidectomy (in 15) or by propyl-thiouracil (in 3) or by methyl-thiouracil (in 2). Four patients (Cases 21–24) received no treatment for thyrotoxicosis.

Thirteen of the 15 patients subjected to subtotal thyroidectomy * showed complete disappearance or great improvement in the angina pectoris for varying periods. In all of these, the thyrotoxicosis was adequately controlled by treatment. One of the remaining two (Case 14) died on the day following subtotal thyroidectomy. The other (Case 13) failed to maintain an initial improvement in his angina pectoris although the thyrotoxicosis was well controlled.

Four of the five patients treated by thiouracil were improved or relieved completely of their anginal attacks. The fifth (Case 20) failed to respond to thiouracil in the dosages used and no significant improvement in the angina pectoris was noted

Thus, of 18 patients whose thyrotoxicosis was controlled by treatment, 17 showed disappearance or marked improvement of angina pectoris. The periods during which the angina was relieved or improved, and the final result or present status of these patients are detailed in Table III.

Four untreated thyrotoxic patients with angina pectoris are included in this series. Two of them (Cases 21 and 22) died suddenly within a few days of diagnosis and before treatment for thyrotoxicosis could be initiated. Treatment was declined by a woman aged 68 (Case 23) who continued to have attacks of cardiac pain until her death two and a half years later. The fourth, a man aged 56 (Case 24), with mild untreated thyrotoxicosis was observed over a period of eight years until his death, which occurred during sleep; in the course of the observation period, his anginal attacks did not alter appreciably in character or severity. The data from these four cases are not sufficient to indicate the course of angina pectoris associated with untreated thyrotoxicosis.

Basal Metabolic Rate

In the untreated state, the basal metabolic rate was less than +40 per cent in 13 and greater than +40 per cent in 11 instances. After treatment by either subtotal thyroidectomy or thiouracil, it was less than +8 per cent in 16 patients. Values of +13 and +25 per cent were obtained in two patients and in the remaining two, the tests were unreliable. Four patients were untreated.

In spite of the paucity of symptoms and signs, the degree of thyroid overactivity in some of the cases was considerable. For example, in Case 19, a man aged 55 with severe angina pectoris, thyrotoxicosis had not been suspected by the referring physician for three years because the cardinal

* Histological examination of the thyroid gland in 13 cases showed diffuse hyperplasia in eleven and hyperplastic nodules in two.

TABLE III

EFFECT OF SUBTOTAL THYROIDECTOMY OR THIOURACIL ON ANGINA PECTORIS ACCOMPANYING THYROTOXICOSIS

Case No.	Duration of A.P. before treatment of thyrotoxicosis (years)	Duration of improvement of A.P. after treatment of thyrotoxicosis (years)	Total years since onset of A.P	Final result
		Subtotal Thyroidectomy Cases		
1	3	8 mo.	5½	8 mo. post-op. developed congest. failure. Died 2½ yr. after op.
2	5	10	15	A.P. returned after 10 yrs. Died suddenly 2 yrs. later.
3	7	10	18	Cong. failure 11 yrs. post-op. and died. Autopsy: old and recent myo. infarcts.
4	2	12	14	Died from cerebro-vascular accident.
5	4 mo.	17	17½	Alive and well. No. A.P.
6	4	17	21	Alive and well. No A.P.
7	6 mo.	11	11½	A.P. returned 11 yrs. after op.
8	4 mo.	8	8⅓	Alive. A.P. on unusual effort.
9	2 mo.	1	1½	Alive and well. No. A.P.
10	1	1	2	Alive and well. No A.P.
11	1 mo.	10	11½	A.P. returned after 10 yrs. relief. Died from myocard. infarct.
12	2	4	10	A.P. returned after 4 yrs. relief. Increased for 4 yrs. Died suddenly.
13	10 mo.	4 mo.	2⅓	Died 18 mo. after operation.
15	2½	5	7	Alive and well. No A.P.
		Thiouracil Cases		
16	6 weeks	2	2½	Alive and well. No A.P.
17	2	1¼	3¼	Alive and well. No. A.P.
18	2	5	7	Alive. A.P. only on unusual effort.
19	8	3	11	Alive. A.P. only on unusual effort.
Average	2·3	6·6	9·4	

symptoms were lacking: yet, the basal metabolic rate was +80 per cent. For a similar reason, thyrotoxicosis had been overlooked in a woman, 42 years old (Case 8), whose basal metabolic rate was +81 per cent.

No consistent correlation was observed between the severity of the angina pectoris * and the pre-treatment level of the basal metabolic rate. Of 20 with severe or moderately severe angina, the basal metabolic rate was less than +40 per cent in 11, and greater than this value in 9 per cent. Two patients with frequent, severe and easily-induced angina pectoris, including pain at rest and frank signs of thyrotoxicosis, were found to have basal metabolic rates of +6 per cent (Case 10) and +12 (Case 11). After subtotal thyroidectomy, the basal metabolic rates fell to −20 per cent and +3 per cent respectively with complete disappearance of the anginal pain and the thyrotoxic symptoms. In both instances, the thyroid glands showed histological evidence of active thyrotoxicosis. The occurrence of thyrotoxicosis with normal low basal metabolic rate is well recognized (Morris, 1931; Plummer, 1931). One of the cases of angina pectoris and thyrotoxicosis reported by Lev and Hamburger (1932) had a basal metabolic rate of −8 per cent.

The basal metabolic rate fell to euthyroid or hypothyroid levels in all the patients whose angina was benefitted by treatment of the thyrotoxicosis. Only one (Case 13) failed to show improvement of his angina following reduction of the basal metabolic rate. Angina persisted unchanged in another (Case 20) after propyl-thiouracil which did not control the thyrotoxicosis. It is clear that the basal metabolic rate alone should not be used as a diagnostic criterion of thyrotoxicosis.

* The severity of the angina pectoris was arbitrarily assessed on the nature of the provocative factors, the frequency of attacks, the occurrence of pain at rest and the response to nitroglycerine.

Blood Pressure

Fifteen of the cases had normal blood pressures (systolic less than 150 mm., diastolic less than 95 mm. Hg.). In five, the systolic and diastolic pressures were elevated, and in four, the systolic pressure only was raised. The average blood pressure for the entire group was 145/90 (men 145/90; women 150/90). The pulse pressure lay between 55–70 mm. in 15 patients; it was below this range in eight and above it in one. It will be noted that the occurrence of hypertension (systolic and diastolic) among these 24 patients with angina pectoris and thyrotoxicosis (33%) is about the same as in angina without thyrotoxicosis (36% White, 1944).

The blood pressure in 16 patients after treatment for thyrotoxicosis was within normal limits in 6, with systolic and diastolic raised in 6, with systolic only in 3, and with diastolic only in one. The average for the group was 160/95 (men 150/90; women 165/100). Thus, while the average blood pressure showed a tendency to increase slightly after treatment for thyrotoxicosis, no characteristic behaviour of the blood pressure was noted in this group of patients.

Since the coronary artery flow depends for the most part on diastolic pressure, and the maximum flow occurs during diastole (Anrep and von Saalfeld, 1933; Wiggers and Cotton, 1933) it might be supposed that angina pectoris would be most likely to occur in those thyrotoxic patients with a low diastolic or wide pulse pressure. For the same reasons, it might be predicted that improvement in angina pectoris following successful treatment of thyrotoxicosis might be reflected in an increase in the diastolic blood pressure with or without a narrowing of the pulse pressure. However, no such correlation was apparent in 13 patients whose blood pressure was recorded repeatedly before treatment and during observation periods of one to eleven years.

Heart Rate

The heart rate was consistently 100 a minute or greater in 17 of the 24 patients (71%) with untreated thyrotoxicosis. In five instances, the rate lay within the range 70–80 a minute despite the presence of active thyrotoxicosis. The average heart rate for the entire 24 patients was 100 a minute (range 72–140 a minute).

Since coronary artery flow is influenced by the duration of diastole, it might be predicted that in those cases of angina pectoris which improved after treatment of thyrotoxicosis, the heart rate would be reduced. Frequent heart rate determinations were made on 12 patients after subtotal thyroidectomy or thiouracil treatment. In 11, the rate was reduced; in the remaining one, the rate remained at 100 a minute and the angina pectoris was not improved, although the other thyrotoxic manifestations were. The average heart rate for these 12 cases with controlled thyrotoxicosis was 80 a minute (range 60–100 a minute). Consequently it is evident that the behaviour of the heart rate in this group of patients is in general similar to that found in uncomplicated thyrotoxicosis. The not infrequent occurrence of thyrotoxicosis with a relatively slow heart rate should be borne in mind.

Electrocardiographic Change

Electrocardiograms were taken in 22 cases. In 7, the tracings were normal. Auricular fibrillation was present in 2 and abnormal T wave inversion in limb or chest leads, or in both, in 4 cases. The signs of myocardial infarction or ischæmia were seen in 5 cases and heart block in 6 (first-degree block and right bundle branch block, one each; left bundle branch block and non-specific intraventricular conduction defects, two each).

Electrocardiograms were taken after treatment by either subtotal thyroidectomy or thiouracil in 15 patients. In 5 of them, the electrocardiogram was improved and in 9 there was no change. In one case, chest leads V1–6 were taken for the first time after propyl-thiouracil therapy and all showed inverted T waves; the limb leads were within normal limits. It is evident that the electrocardiogram plays only a limited role in the diagnosis.

A number of these patients were seen for the first time before multiple chest leads had come into routine use. However, 6 of the 7 patients with normal electrocardiograms in the untreated state had multiple chest leads taken, usually V1–6, or at an earlier date CF 1–6. In a few cases, the three unipolar extremity leads were included. Standard limb leads only were recorded in Cases 6 and 7 which showed abnormal patterns before operation and reversion to normal afterwards. It is possible that some residual abnormality would have been uncovered in these cases by multiple chest leads.

Reversion from an abnormal to a normal electrocardiogram is illustrated in Fig. 1. This

FIG. 1.

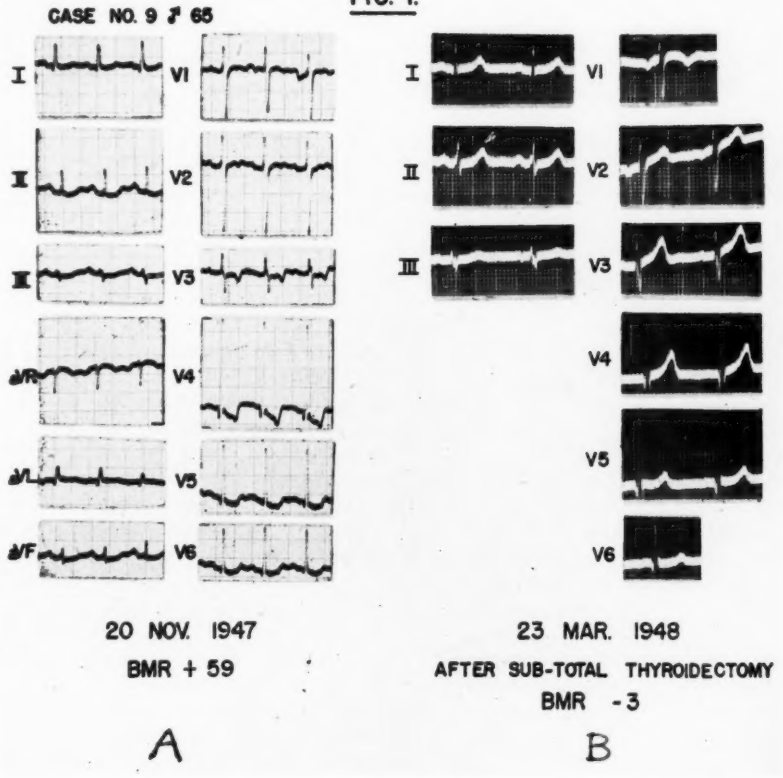

FIG. 1.—(A) Before subtotal thyroidectomy. Sinus tachycardia, depressed S–T in leads I, II, III, V3–6, and inverted T waves in V3–4. (B) After subtotal thyroidectomy. Normal electrocardiogram.

man, aged 65 (Case 9), complained for 2 months of anginal pain which came on at rest or with exercise. Symptoms of thyrotoxicosis had been present for 18 months but overlooked by the attending physician, and the basal metabolic rate was +59 per cent. After subtotal thyroidectomy the thyrotoxic manifestations subsided and up to the present time, one year after operation, the patient has not experienced any anginal attacks and is at work daily. An electrocardiogram (Fig. 1A) taken before operation showed sinus tachycardia, depression of the S–T segment in leads I, II, III,

and V3–6 with T wave inversion in V3–4. The record taken one year after operation (Fig. 1B) was within normal limits.

Heart Size

In 23 instances, X-ray examination of the heart was carried out. In 12, the heart size was normal and in 11 it was enlarged. Six of the latter showed slight enlargement, and 5, moderate enlargement.

After treatment for thyrotoxicosis, two slightly enlarged hearts (Cases 12 and 16) became normal, and one moderately enlarged heart (Case 20) was reduced in size but was still outside normal limits. In the remaining cases, the heart size was unchanged after treatment.

The Nature of Angina Pectoris Co-existing with Thyrotoxicosis

Since a high percentage of patients with angina pectoris and thyrotoxicosis can be benefitted by controlling the thyrotoxicosis, we have reviewed carefully the histories and clinical features of angina pectoris in this series to determine whether they differed from non-thyrotoxic anginal cases in any respect that might give a clue to the association of the two conditions. The presence of any distinguishing feature would be of special importance in view of the subclinical or masked nature of the thyrotoxicosis referred to above, which is found commonly in these patients. We were unable to note anything unusual in the quality, site, radiation or duration of the pain, and the response to nitroglycerin was usually prompt. Three features, however, impressed themselves on us. Anginal pain occurring at rest, usually when the patient was in bed (angina pectoris decubitus) and sometimes awakening him from sleep, was noted in 18 of our 24 patients (75 %), all of whom also had effort pain. This symptom is not uncommon in euthyroid cases with coronary insufficiency, and was described in over 60 per cent of 103 cases of syphilitic angina pectoris (Jones and Bedford, 1943). Nevertheless, its prominence in our thyrotoxic patients suggests that sometimes it may assume added significance by pointing to the possible co-existence of thyrotoxicosis. The second feature which impressed us was the recent onset of angina in many of the cases; in 7 patients, the pain appeared for the first time less than 6 months before examination, and in 2 others, 10 months previously. Of itself, this fact is not of much significance, but if within a period of weeks or months, angina appears and rapidly progresses in frequency of occurrence and severity, and especially if the attacks come on at rest, diligent search should be made for a thyrotoxic element in the case. The third noteworthy feature which is unique in angina pectoris in thyrotoxic subjects, is the lessening in the frequency and often abrupt cessation of anginal attacks and especially of angina decubitus, following the administration of thiouracil, or of iodine as a preliminary to subtotal thyroidectomy or thiouracil therapy. In several of our cases, the sudden cessation of attacks following the use of thiouracil or iodine occurred after long control periods of rest and other medication.* We were well aware that a degree of improvement is to be expected at least for a time in certain cases of angina from almost any remedy, as has been convincingly demonstrated by Evans and Hoyle (1933). In the thyrotoxic patients with angina, however, the relief from anginal attacks following thiouracil or iodine therapy goes hand in hand with the suppression of the thyrotoxic symptoms, and as demonstrated in the majority of our cases the improvement in angina persists when the thyrotoxicosis is controlled by operation or anti-thyroid drugs.

In euthyroid patients with coronary artery disease, angina pectoris may undergo remissions which on rare occasions may last for years. Such remissions, which according to Gallavardin (1924), are found in eight per cent of cases, may be the sequal to a myocardial infarction or may be observed in the course of administration of placebos (Evans and Hoyle, 1933). In the 18 patients (7 dead † and 11 living) of this series in whom the thyrotoxicosis was adequately controlled, the

* Since this study was completed, we have encountered a woman, aged 59, with proven thyrotoxicosis of six months' duration and angina pectoris for four weeks including angina decubitus. Under controlled hospital conditions, the anginal attacks subsided within 12 hours of administering 150 mg. of propyl-thiouracil, and did not return.

† Cases 2 and 12 died suddenly, Cases 3 and 11 after recent myocardial infarction, Case 4 from a cerebrovascular accident, Case 1 from congestive failure and Case 13 unknown.

average duration of improvement of the angina was 6·6 years (range 4 months–17 years); in the 7 dead, the average duration of improvement was 6·7 years (range 4 months–12 years), and in the 11 living, 6·6 years (range 1–17 years).

In Table IV, the duration of life from the onset of angina pectoris in the 18 treated thyrotoxic cases is compared with the corresponding figures in two series of angina pectoris without thyrotoxicosis (Eppinger and Levine, 1934; White, Bland and Miskall, 1943).

Any discussion concerning the prognosis of angina pectoris and thyrotoxicosis must be qualified by the limitation imposed by the small number of patients in our series, and the survival periods do nothing more than represent a trend from which no far-reaching conclusions should be drawn.

TABLE IV

DURATION OF LIFE IN ANGINA PECTORIS: EUTHYROID PATIENTS COMPARED WITH TREATED THYROTOXIC PATIENTS

	No. of cases	Average duration of life (years)		
		To death	In living	In living and dead
		Euthyroid Patients		
Eppinger and Levine (1934)	141	4·6 (141)	—	—
White, Bland and Miskall (1943)	497	7·9 (445)	18·4 (52)	9·1
		Treated Thyrotoxic Patients		
Present Series	18	10·9 (7) (2·3 to 18)	8·6 (11) (1·5 to 21)	9·4 (1·5 to 21)

Table IV shows that the average survival time after the onset of angina in our seven fatal cases exceeds considerably the corresponding times for the non-thyrotoxic cases. The part played by treatment of thyrotoxicosis in increasing the survival time of these patients is difficult to assess without corresponding figures on a series of angina pectoris with untreated thyrotoxicosis, and such a series would be almost impossible to come by.* However, since the evidence is clear that thyroid overactivity puts an added prolonged burden on the heart, increasing its rate (Boas, 1932), size (Kepler and Barnes, 1932), oxygen consumption (Andrus, 1932) and minute output, and may lead to congestive failure in otherwise normal hearts (Levine, 1930; Kepler and Barnes, 1932), it is safe to assume that removal of such a burden from a heart already diseased by coronary arteriosclerosis would be advantageous.

The increased survival time may be conceivably a reflection of the earlier appearance of angina pectoris when thyrotoxicosis is also present; in these cases the latter condition may give rise to coronary insufficiency with a degree of coronary arteriosclerosis which would be asymptomatic in the individual with normal thyroid function.

The high incidence in this series of angina at rest, especially in bed (angina pectoris decubitus) (75%) might be cited as an indication of the severity of the coronary insufficiency in our cases. White, Bland and Miskall (1934), studying 103 cases of angina decubitus, found no significant difference in the average duration of disease to death, or between the average survival period, in the living cases in this group and that of the group of angina pectoris as a whole. However, in an additional series of 75 cases of angina decubitus, 47 of whom were followed to death, the average survival period after the onset of the decubitus pain was only 2·8 years. Six of our seven patients with treated thyrotoxicosis who died had angina decubitus in addition to angina of effort. The survival periods of these six patients from the onset of the decubitus type of pain until death are not known exactly, but when estimated from the beginning of treatment until death, an average survival period of 8·1 years (range 2 to 12 years) is found. Since angina decubitus had been present for weeks

* Two of our patients with mild angina and untreated thyrotoxicosis (Cases 23 and 24) lived for two and a half years (B.M.R. +68%) and eight years (B.M.R. +25%) respectively, after the onset of pain.

or months before treatment was begun, the true survival period from the onset of decubitus pain would be longer. In two patients (Cases 11 and 12), after many years of complete relief from attacks of angina decubitus recurred and persisted for two years before death. In 9 surviving patients who had angina decubitus, the average survival time since onset of treatment was 6 years (range 1 to 17 years), and for reasons mentioned above, this figure is an approximation which underestimates the true survival period. Hence, the evidence presented, if limited, is indicative that angina decubitus occurring with thyrotoxicosis does not carry with it the ominous prognosis of this symptom in euthyroid patients, and with adequate control of the thyrotoxicosis it may be dispelled for many years.

In the majority of cases of angina pectoris associated with thyrotoxicosis, the underlying cardiac lesion is coronary arteriosclerosis. In addition, certain pathological changes in the myocardium have been reported in patients dying from thyrotoxicosis. The nature and significance of these changes have been discussed fully by McEachern and Rake (1941). Coronary arteries with a relatively mild degree of arteriosclerosis, too slight to interfere with the blood supply of the heart in the euthyroid patient, may be unable to meet the demands of the increased metabolic rate of the heart in thyrotoxicosis, with its increased oxygen consumption, stroke volume and cardiac output. If the metabolic rate be reduced by treatment, the degree of relative coronary insufficiency will be lessened. Angina may then diminish or disappear, until with the natural advance of the arteriosclerotic process, coronary insufficiency and angina eventually return.

Duchosal and Henny (1941) have reported a case of angina pectoris occurring in a thyrotoxic subject in the absence of coronary arteriosclerosis. A woman, aged 50, complained of chest pain occasioned by slight effort, eating, emotion and especially when in bed. Thyrotoxicosis was present, the basal metabolic rate being +51 per cent. With exercise, the electrocardiogram showed QRS, S–T and T wave changes similar to those seen in acute posterior myocardial infarction. On resting, these changes disappeared gradually. The attacks subsided immediately after a course of Lugol's iodine was begun. Ligation of the superior thyroid arteries was carried out but the patient died suddenly six hours after the operation. At autopsy, the coronary arteries were shown to be normal and no myocardial infarcts were found. The myocardium contained numerous small foci of degeneration surrounded by hyperæmic zones, some of which contained areas of fibrosis. The authors suggested that these foci liberated a pain-producing substance (P-substance) which was responsible for the pain either directly or indirectly by bringing about vascular spasm. The latter possibility was supported by the relief which followed the use of nitroglycerin.

Several of our cases ran a course similar to that quoted above:

> Case 5. A male school teacher, aged 31 years, was first seen in 1931 complaining of chest pain characteristic of angina pectoris which had appeared 4 months previously. The attacks occurred on effort and at rest, and became so frequent that he considered retiring from his occupation. He also complained of recent diarrhœa and palpitation. It was noted that he had tachycardia, soft sweaty skin, slight thyroid enlargement and a digital tremor. The basal metabolic rate fell from +27 to +7 per cent with Lugol's iodine and at the same time, the attacks ceased. Sub-total thyroidectomy was performed in January 1932, and histological examination showed a diffusely hyperplastic gland. The following year, the basal metabolic rate was −23 per cent with no symptoms of hyperthyroidism. At a recent routine examination (May 1949), 17 years later, the patient stated he had had no recurrence of chest pain and could play 18 holes of golf without discomfort. He has been in full-time employment since his operation. Clinical examination revealed a raised blood pressure (170/115) but otherwise nothing abnormal; the electrocardiogram was normal.

While we have no pathological evidence to confirm the ætiological concept of anginal pain advanced by Duchosal and Henny, the immediate freedom from pain after subtotal thyroidectomy and its failure to reappear for as long as 17 years in several of our cases, suggests that some process other than coronary arteriosclerosis may be the basis of angina pectoris occurring in certain thyrotoxic patients. The prompt relief from attacks of cardiac pain in several of our patients on starting thiouracil treatment before the basal metabolic rate began to fall, and following a control period of

bed rest or unsuccessful treatment with other medications is additional evidence implying the possibility of a toxic effect of thyroid secretion on the myocardium.

Summary

The association of angina pectoris and thyrotoxicosis has been studied in 24 patients (18 men and 6 women).

Two outstanding features of the anginal pain were (*a*) the frequency of angina pectoris decubitus, which was present in 18 of the 24 patients (75%), and (*b*) the immediately beneficial response to iodine used preparatory to subtotal thyroidectomy or thiouracil.

The symptoms of thyrotoxicosis were fewer and less prominent than in a series of patients with thyrotoxicosis without angina previously described. Possible reasons for the difference are discussed.

Twenty of the 24 patients were treated by either subtotal thyroidectomy (15) or thiouracil (5) (propyl-thiouracil in 3 and methyl-thiouracil in 2). In four patients, the thyrotoxicosis was untreated.

Thirteen of the 15 patients subjected to subtotal thyroidectomy showed complete disappearance or marked improvement of the angina for periods ranging from eight months to 17 years. Four of the five patients treated with thiouracil were benefited similarly for one and a quarter to five years. The average duration of complete relief or improvement of angina in the treated group was 6·6 years. In several instances, the attacks returned after periods of freedom ranging from 4 to 11 years.

The clinical features are described and the pathological physiology discussed.

The average duration of life in seven fatal cases of angina pectoris and thyrotoxicosis was 10·9 years, compared with 7·9 years and 4·6 years respectively in two series of angina pectoris without thyrotoxicosis previously reported. Possible reasons for the longer survival in the thyrotoxic cases are discussed.

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CARDIAC ANOMALIES IN MONGOLISM

BY

PHILIP RAINSFORD EVANS

From the Hospital for Sick Children, Great Ormond Street, London

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In a well-known textbook Maud Abbott is credited with the opinion that " the commonest cardiac anomaly in Mongolian idiocy is a defect of the interauricular septum, especially ostium primum." Reference to her paper shows that she actually wrote that in mongols the defect " in our experience is not infrequently of this type " (Abbott, 1924). She described one case, in which there was also a ventricular septal defect that divided the aortic cusp of the mitral valve.

This addition is suggestive of persistent atrioventricularis communis, of which Taussig (1947) wrote: " The diagnosis is based on the law of probability. If a Mongolian idiot has a congenital malformation of the heart which superficially resembles a ventricular septal defect and there is no cyanosis, the overwhelming probability is that he has a patent atrioventricularis communis. The demonstration of an abnormally low oxygen saturation of the arterial blood clinches the diagnosis." Robson (1931), Meecker (1935) and Robinson (1941), have described examples. Goetsch's patient showed the same lesion and dextroposition and infantile coarctation of the aorta (Goetsch, 1938), while two patients described by Gunn and Dieckmann (1927) showed mongolism, persistent atrioventricularis communis and patent foramen ovale, with patent ductus arteriosus also in one case.

One might easily get the impression that persistent atrioventricularis communis was the usual cardiac lesion of mongolism, in spite of the description of the single cases with other anomalies by Wolf and Levinson (1939) and Mannheimer (1949). However, Leech (1935) described six cases, only one of which had this defect, with patent foramen ovale and anomalies of the great vessels in addition. Writers on mongolism (e.g. Benda, 1946, and Engler, 1949) do not make numerical statements about the frequency of the lesions they mention. The examination of a larger series than that of Leech would seem to be worth while.

Between January, 1911, and October, 1949, necropsies were done at the Hospital for Sick Children, Great Ormond Street, on 63 mongols, and in 28, cardiac anomalies were described. The records are not impeccable, for until 1942 necropsies were not made by a trained morbid anatomist, but by the Medical Registrar and Pathologist, who was selected for the three years' appointment because of clinical competence and ability. The diagnosis of mongolism is likely to have been right in every case, but the descriptions of the cardiac lesions must be viewed critically. In many cases they are excellent. However, in analysing the findings, " probe," " physiological " or similar slight degrees of patency of the foramen ovale at all ages, and all but wide patencies of the ductus under the age of one year have been omitted. " Patent foramen ovale " has not been taken at its face value, as in earlier years there may have been confusion with persistent ostium primum.

In the period reviewed, children under 12 years of age, suffering from all types of acute disease (except infectious fevers) and many chronic medical and surgical conditions were admitted. Judging by the clinical summaries, congenital heart disease was the major cause of death in seven mongols, broncho-pneumonia in another nine, and extracardiac congenital anomalies in three. The age at death was rather similar in mongols and other children with congenital heart disease (Table I). Nine of the mongols with heart disease showed other congenital anomalies: Meckel's diverticulum

TABLE I

AGE AT DEATH IN MONGOL IMBECILES WITH AND WITHOUT CONGENITAL HEART DISEASE, AND IN OTHER CHILDREN WITH CONGENITAL HEART DISEASE

Death in	Mongol		Other children with morbus cordis
	With morbus cordis	Without morbus cordis	
1st month	4	5	6
2nd–5th month ..	16	7	35
6th–11th ,, ..	6	7	5
2nd year	1	7	2
3rd ,, ...	0	4	0
4th ,, ...	0	4	0
5th ,, ...	1	0	1
6th ,, ...	0	1	0
7th ,, ...	0	0	1

in three, abnormal pulmonary fissures in two, atresia of the common bile duct, bifid rib, cleft palate, symphalangy, œsophageal atresia with œsophagotracheal fistula, hydrocephalus, spina bifida with meningocele, ectopic anus, duodenal atresia, and intestinal malrotation, each in one instance.

The anomalies found in these 28 hearts are surprisingly various (Table II). Interestingly enough, persistent atrioventricularis communis was found only 4 times, and even allowing for unfamiliarity with the condition, it must have been absent in at least 21. On the evidence produced by these 28 and Leech's 6 cases, persistent atrioventricularis communis should not be regarded as the typical cardiac lesion of mongolism, for it occurred in only 5 of the total of 34. Application of the " law of probability " mentioned by Taussig leads to the conclusion that " if a Mongolian idiot has a congenital malformation of the heart which superficially resembles a ventricular septal defect and there is no cyanosis," the probability is that he actually has a ventricular septal defect, although he may have the less common persistent atrioventricularis communis.

TABLE II

CARDIAC ABNORMALITIES FOUND IN 28 MONGOLS

	Without patent ductus arteriosus	With patent ductus arteriosus
Large atrial septal defect, type uncertain	5	—
Persistent ostium primum	1	—
Persistent ostium primum and secundum	—	1
Absent auricular septum	1	—
Persistent atrioventricularis communis	3	1
Large atrial septal defect, and ventricular septal defect (membranous)	1	2
Ventricular septal defect (membranous 6, more extensive 1)..	6	1
Patent ductus arteriosus	—	1
Pulmonary infundibular stenosis	1	—
Pulmonary artery stenosis, atrial septal defect ..	—	1
Fallot's tetralogy (1 with atrial septal defect) ..	2	—
Aberrant right subclavian artery	—	1

In the 28 hearts there were 47 anomalies of the heart or great vessels (Table III). Atrial and ventricular septal defects each accounted for just over one-third, and patent ductus arteriosus for one-sixth. Most of the remaining lesions were pulmonary stenoses. Defect of the pars membranacea of the ventricular septum is the commonest anomaly. Owing to uncertainty about the

TABLE III

FREQUENCIES OF INDIVIDUAL ANOMALIES IN THE HEARTS OF 28 MONGOLS WITH CONGENITAL HEART DISEASE

Auricular septum, all defects			17
,, ,,	absent	1	
,, ,,	persistent ostium primum	2	
,, ,, ,, ,,	secundum	1	
,, ,, ,,	atrioventricularis communis	4	
Ventricular septum, all defects			17
,, ,,	persistent atrioventricularis communis	4	
,, ,,	membranous defect	12	
,, ,,	absence of four-fifths	1	
Ductus arteriosus, widely or persistently patent			8
Pulmonary stenosis			4
,, ,,	infundibular	1	
,, ,,	arterial	1	
,, ,,	infundibulo-arterial	2	
Aberrant right subclavian artery			1

precise nature of the atrial septal defects it is impossible to decide whether persistent ostium primum is a very close runner-up, or merely a bad second. Probably patent ductus comes third, while pulmonary stenosis and persistent atrioventricularis communis are bracketed in the fourth place. Other lesions were inconsiderable in this series.

This examination of records showed that no particular combination of anomalies was characteristic of the abnormal heart in mongolism, but it did not indicate whether the uncommon lesion of persistent atrioventricularis communis was in fact a peculiarity of the disease.

The necropsy records of fifty children, who were not mongols but who had congenital anomalies of the heart were therefore examined. They were chosen from the same twenty volumes of post-mortem reports as the mongols, the first two or three cases (depending on whether there were more or less than the average number of mongols in that particular volume) being selected from each. The list (Table IV) demonstrates the amazing variety of congenital heart disease in patients dying in a children's hospital.

Among the individual lesions (Table V), the absence of persistent atrioventricularis communis is noteworthy: it appears to be less rare in mongols than in other children with congenital heart disease. Auricular septal defect in general is probably unduly common in mongols, while ventricular septal defect and patent ductus are not. On the other hand, transposition of the great vessels seems to be unusual in mongolism, although Mannheimer's case must not be forgotten (Mannheimer, 1949). The non-occurrence of truncus arteriosus and of aortic coarctation in the mongols is notable, although the series is small. The adult type of coarctation is not likely to be encountered often in the autopsy records of a children's hospital, but clinical experience also indicates that it is uncommon in mongols. The relatively higher figure for pulmonary stenosis in the mongols is rather surprising. It is, of course, possible that the prognosis of mongols with pulmonary stenosis, atrial septal defect, or persistent atrioventricularis communis is worse than that of other patients with these cardiac anomalies, who may come to necropsy in a hospital for adults. The figures presented here show the incidence of different congenital abnormalities of the heart in patients dying young, rather than in all patients.

The most clear-cut difference between the lesions in the two series is the absence of defects due to malrotation of the bulbus cordis (except Fallot's tetralogy) in the mongols, and of a common atrioventricular opening in the other children. In this series atrial septal defects (which may have been due to persistence of the ostium primum) were commoner in the mongols than in the other

TABLE IV

CARDIAC ABNORMALITIES FOUND IN 50 PATIENTS WHO WERE NOT MONGOLS

	Without patent ductus arteriosus	With patent ductus arteriosus
Atrial septal defect (1 certainly ostium primum)	3	1
Ventricular septal defect	5	3
Patent ductus arteriosus	—	7
Atrial and ventricular septal defects	1	1
Bilocular heart, subaortic atresia	—	1
Bilocular heart, severe pulmonary artery stenosis, single pulmonary vein	1	—
Trilocular biatrial heart, atrial septal defect	1	—
Trilocular biventricular heart	1	—
Trilocular biventricular heart, atrial septal defect (1 with mitral atresia)	1	1
Hypoplastic left auricle and ventricle	1	1
Tricuspid atresia with non-functioning right ventricle, atrial and ventricular septal defects	1	—
Truncus arteriosus, over-riding interventricular septum (1 with atrial septal defect)	2	—
Truncus arteriosus from right ventricle, ventricular septal defect	2	—
Transposition of aorta and pulmonary artery (1 in each group with atrial septal defect and 1 in each group with V.S.D.)	4	1
Transposition of aorta, pulmonary artery over-riding ventricular septum	1	—
Pulmonary artery stenosis, atrial septal defect, ventricular septal defect	1	—
Pulmonary artery stenosis, ventricular septal defect	—	1
Coarctation of aorta, infantile type	—	2
Coarctation of aorta, adult type (1 with ventricular septal defect)	2	—
Situs inversus of heart alone (1 with atrial and 1 with ventricular septal defect)	2	—
General hypertrophy	1	—
	50	

TABLE V

INDIVIDUAL ANOMALIES OCCURRING 2 OR MORE TIMES IN THE HEARTS OF 28 MONGOLS, OR 4 OR MORE TIMES IN 50 PATIENTS WITH CONGENITAL HEART DISEASE WHO WERE NOT MONGOLS

Lesion	Mongol		Not mongol	
	No.	Percentage	No.	Percentage
Auricular septum, all defects	17	60	18	36
Auricular septum, ostium primum or secundum, without persistent atrioventricularis communis	12	43	15	30
Persistent atrioventricularis communis	4	14	0	0
Ventricular septum, all defects	17	60	26	52
Ventricular septum, absent or nearly so	1	4	5	10
Ventricular septum, membranous defect without persistent atrioventricularis communis	12	43	21	42
Patent ductus arteriosus	8	29	20	40
Truncus arteriosus	0	0	4	8
Pulmonary stenosis	4	14	3	6
Coarctation of aorta	0	0	4	8
Transposition of aorta and pulmonary artery	0	0	7	14

children, ventricular septal defects were equally common in the two groups, while patent ductus arteriosus was less common in the mongols. The common atrioventricular canal is divided and the ostium primum is closed at about the 41st day of intrauterine life; the interventricular foramen closes at about the 47th day (Hamilton, Boyd, and Mossman, 1945); the second torsion of the bulbus occurs between the fifth and eighth weeks (Brown, 1939) so that exaggerated torsion may occur after the 56th day; the ductus arteriosus closes after birth. Comparison of this time table with the lesions found in or absent from the mongol series supports Abbott's suggestion that the defects of development in mongols occur early (Abbott, 1924).

Summary

Congenital heart disease was found in nearly half of a series of mongol imbeciles dying in the first five years of life. In the records of 63 autopsies, 28 examples were found.

Ventricular and atrial septal defects each accounted for one-third of the individual lesions, and patent ductus arteriosus for one-sixth. Pulmonary stenosis and persistent atrioventricularis communis each occurred in 4 patients.

Compared with other children with congenital heart disease dying in the same hospital in the same period, transposition of the great vessels, coarctation, and truncus arteriosus seemed to be unassociated with mongolism. Atrial septal defects and pulmonary stenosis were more common in the mongols than in the other patients. Speaking generally, the cardiac anomalies in mongolism appeared to be due predominantly to defects occurring in the earlier stages of cardiac development.

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EMBOLISM IN MITRAL STENOSIS

BY

GEOFFREY BOURNE

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A man was examined for a railway company because his disability had been ascribed to his employment. He had felt quite well and had been able to perform his work as an electrician until three months before he was examined, when he was suddenly struck down in the course of his routine work by an attack of left-sided weakness. Physical examination proved that this was due to cerebral embolism secondary to mitral stenosis. It was claimed that this embolism was due to physical effort. A search throughout many textbooks and articles gave no solution to the question of the relationship between exercise and embolism in this disease, and further cases met with in the course of practice were therefore subsequently tabulated in order to attempt to find an answer.

Relationship of Exertion to Embolism

The series forming the basis of this study is one of 29 patients in all, with 31 embolic incidents, two of the patients having suffered from two separate emboli separated from one another by a space of time. It is often assumed that embolism in mitral stenosis occurs only in patients in whom auricular fibrillation is present: this is not universally true. In the present series of 29 cases, 6 showed regular rhythm and 23 auricular fibrillation. The relationship of embolism to blood flow through the auricles and to exercise generally is interesting. Embolism occurred very much more frequently in patients who were ambulatory, and quite rarely in patients whose activities were restricted by the presence of congestive failure. The degree of mobility was as follows: 24 of the embolic incidents occurred in patients who had good exercise tolerance, being normally ambulatory although restricted slightly by a little shortness of breath; 4 of the incidents were in patients who were ambulatory, but had a poor exercise tolerance although signs of congestive failure were absent; and 3 of the incidents were in patients who had signs of congestive failure at the time of embolism.

These facts would at first suggest that exercise as such might be a factor in the causation of embolism when a clot is present in the left auricle; on the other hand, an analysis as to the time of onset of the embolism points to a contrary conclusion. Only twice in the whole series did an embolism occur while the patient was actively mobile. The first of these was a man with regular rhythm aged 45, who was a machine operator in active employment: he had walked on the flat to get two mugs of tea for himself and his mate; and on his return, on reaching for a spanner, he found his hand had become weak. The second was a woman, a railway porter, of 41 whose heart rhythm was also regular; whilst walking on the platform she was forced to sit down, finding that her left arm and leg had suddenly become weak.

Seven of the cases, all with auricular fibrillation, were seized by the effects of embolism while undertaking very easy physical exercise. The individual circumstances were as follows: sudden weakness of the arm occurred while engaged in brushing his hair in a man of 65; weakness of her right side overtook a woman of 45 while she was kneeling, taking cinders out of her grate; a woman of 34 suddenly became weak in her arm and leg whilst sitting, talking to a friend; a woman of 41 had sudden right-sided weakness while making tea; a woman of 45 suffered sudden numbness down her left side while she was walking about her house, having been rather more busy than usual; and a

woman of 41 had a sudden right hemiplegia while she was standing up at home. Thirteen of the whole series of patients suffered from hemiplegia or other embolic symptoms while sitting down, and nine of them while alseep in bed.

The position of the embolic lesions was as follows: 22 of them were cerebral; 3 were popliteal and one each was axillary, femoral, retinal, splenic, and mesenteric. There was no renal embolism in this series.

Discussion

Embolism in mitral stenosis has become a subject of increased importance since the introduction of anticoagulant therapy. A recent paper on resection of the left auricular appendix by Madden (1949) also raises the question as to whether patients liable to embolism are likely to be satisfactory subjects, either as regards surgical risk or as regards post-operative expectation of life. The third point of practical importance, in reference to compensation cases, has been already referred to at the commencement of this paper.

In patients with mitral stenosis in whom the narrowing is great or very considerable, there is an accumulation of blood in the left auricle, which chamber is therefore more distended than normal. When regular rhythm is present and the auricles are contracting, there is an accentuation in the onward flow of blood from left auricle to left ventricle during auricular systole, and in proportion to the degree of stenosis the chamber remains to some degree distended most of the time. When auricular fibrillation supervenes this state of auricular distention becomes permanent. The effect of permanent or nearly permanent auricular distention upon sessile clot in the chamber would be that such clot remains undisturbed or very little disturbed by the flow of blood in the chamber and by variations of pressure. If mitral disease with little narrowing of the mitral ring is considered, this mitral ring having been made rigid or somewhat rigid by chronic rheumatic endocarditis, a different physical state must occur. In proportion to the wideness of the mitral ring there will be a sudden rise of interauricular pressure at the time of left ventricular systole, due to mitral regurgitation. Here there will be both a diastolic flux and a systolic reflux of blood, similar to that of sea-water flowing in and out of a rock pool fed from above, as the tide begins to fill it. Clot in this case, unless it is closely adjacent to the wall, would stand a far greater chance of being moved to and fro, fragmented, and washed free into the blood stream. Catheterization of the left auricle being at the moment impossible of attainment, it is not feasible to check the left auricle pressures by practical experiment on the living human heart, but the facts stated seem to admit of no other explanation, and they also are compatible with the clinical observations made in the above series of cases.

The following conclusions as regards the likelihood of embolism in mitral stenosis seem to be legitimate. Embolism is not directly related to physical effort or exertion. Embolism is not usually due to clot formation in the dilated auricle of severe congestive failure. Embolism is commonest in patients whose exercise tolerance is good or very fair, and in whom the mitral orifice is therefore relatively large, allowing a considerable degree of regurgitation in addition to a slight or only moderate degree of stenosis.

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VENTRICULAR SEPTAL DEFECT IN EARLY CHILDHOOD

BY

R. M. MARQUIS *

From the Royal Infirmary, Edinburgh

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A particular group of children in whom a defect of the ventricular septum leads to cardiac disability in early life is the subject of this paper. The clinical picture that serves to distinguish the graver disability from the better known maladie de Roger is outlined.

The Maladie de Roger—Clinical Features

The maladie de Roger has been a well-recognized clinical entity since the characteristic parasternal murmur was first described (Roger, 1879). The absence of symptoms and the presence of striking physical signs have been taken as the essential points in the diagnosis (Muir and Brown, 1934). In the routine examination of school children, follow-up studies have confirmed the clinical impression that the isolated ventricular septal defect may be regarded as a benign lesion. As with Roger's original cases, repeated examination has revealed no clinical deterioration and no change in the physical signs. Commonly there is no significant radiological or electrocardiographic alteration during the school period (Perry, 1937). Such patients may lead useful, energetic lives and, provided they escape subacute bacterial endocarditis and other incidental diseases, die of congestive heart failure in middle or later life. Roger's oldest case was a woman of 50 years who had borne four children and was leading an unrestricted life; cases recognized as having congenital heart disease in infancy have been followed to over 70 years of age (Gilchrist, 1948).

The Ventricular Septal Defect—Autopsy Features

Pathological confirmation in the maladie de Roger is rare. Roger's contribution to medicine is all the more remarkable in that he did not have the opportunity to confirm the diagnosis in any one of his cases. None of Muir and Brown's (1934) cases had autopsy confirmation, and only two of Perry's cases had died at the time he gave his paper (1937). The first case diagnosed clinically to be proved post-mortem was a boy of 4 years who died from diphtheria (Dupré, 1891). The defect usually occurs through the muscular septum just anterior to the membranous septum. It is circular or oval in shape and its margins are surrounded by fibrous tissue. It opens into the right ventricle behind the septal cusp of the tricuspid valve. The size of the defect varies from a minute opening to 1 cm. in its longest diameter (Abbott, 1936; Brown, 1939).

In sharp contrast to the benign clinical picture of the symptomless lesion, post-mortem statistics show that the ventricular septal defect alone, or in combination with some other minor flaw, has in fact a high mortality in infancy and early childhood. Of Abbott's 50 cases, no less than 21 died at or under 5 years of age (Bauer and Astbury, 1944). Of 110 consecutive cases of congenital heart disease coming to autopsy during the first three years of life in the Royal Hospital for Sick Children, Edinburgh, no less than 28 (25%) had such defects of the ventricular septum. This malformation thus constituted the commonest single lesion in this post-mortem series.

* Kirk Duncanson Research Fellow of the Royal College of Physicians, Edinburgh.

The malformation may be similar to that in the maladie de Roger, or there may be some relatively minor difference. The associated flaws, slight in themselves, take a variety of forms.

(1) Incompetence of the tricuspid valve through adherence of its septal cusp to the defect (Abbott, 1927; Muir and Brown, 1934).

(2) Incompetence of the aortic valve through involvement of the adjacent cusp in the defect (Laubry, Routier, and Soulié, 1933).

(3) The defect may be high, the aortic septum failing to meet the ventricular septum, and the blood from the high pressure left ventricle is pumped almost directly into the pulmonary artery.

(4) The defect may be larger than 1 cm. in its longest diameter.

(5) The defect may be situated between the aortic valve and an anteriorly rotated mitral valve; this variation is occasionally associated with a partial subaortic stenosis (Taussig, 1947).

(6) The aorta may be slightly hypoplastic.

(7) The defect may replace the membranous septum (MacGregor, 1949).

The cause of death in the simplest cases is generally an incidental disease, such as gastro-enteritis, but in the particular group to which attention is directed, the malformation of the heart is itself responsible for death.

Case Records

Four cases are reported to illustrate the clinical features of this particular group in which the ventricular septal defect gives rise to considerable difficulties and may lead to death from congestive failure within the first few years of life. The presence of this malformation was confirmed post-mortem in the first two cases.

Case 1. Female, aged 2½ years. Admitted to hospital in congestive heart failure. Walked at 14 months. Liable to respiratory infections; easily tired and breathless.

On examination, underweight (19½ lb.) in spite of congestion. Dyspnœic at rest, prominent sternum, deep Harrison's sulci. Tachycardia, 140 a minute. B.P. 130/95. Gross cardiac enlargement. No thrills. Coarse, grating, systolic murmur, maximal in second and third intercostal spaces at left sternal margin. Pulmonary second sound grossly accentuated. Liver enlarged. Lungs congested, but no peripheral œdema. Tinge of cyanosis on admission cleared with rest.

Gross, generalized cardiac enlargement on radioscopy (Fig. 1) with congestion of pulmonary vessels. Highly unusual cardiogram (Fig. 2), typical of neither isolated right nor isolated left ventricular hypertrophy.

Temporary improvement followed by increasing dyspnœa and death. At necropsy immense cardiac enlargement (Fig. 3). Entire anterior surface occupied by right ventricle. Equal degree of hypertrophy and dilatation of both ventricles. Slight dilatation of right atrium, none of left. Left auricular

Fig. 1.—Radiograph (anterior) of Case 1 at two and a half years. Gross, generalized cardiac enlargement. Congested lung fields.

appendage rotated anteriorly. Slight aortic hypoplasia. Pulmonary artery double the size of aorta. A large ventricular septal defect with fleshy margins replacing membranous septum and large part of anterior muscular septum; situated between aortic and anteriorly rotated mitral valve and 3 cm. in its longest diameter. Chordæ of anterior mitral cusp originating from anterior margin of defect. Partial subaortic stenosis not apparent. All valves competent. Pulmonary congestion and commencing hypostatic pneumonia.

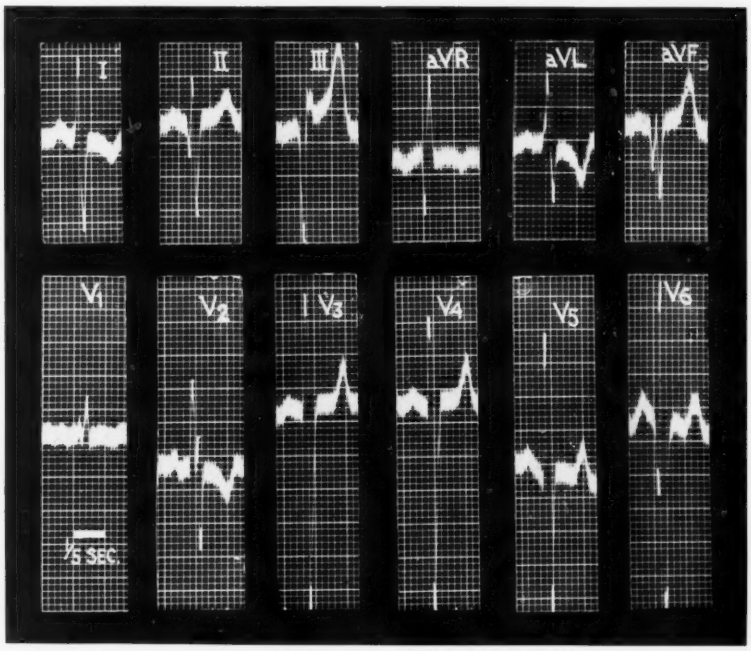

FIG. 2.—Electrocardiogram of Case 1 at two and a half years. Deep S wave in lead 1; notched R wave as sole initial deflection in V1, tall R wave in aVR and deep S wave in V6 are suggestive of right ventricular hypertrophy; deep Q and tall R wave in V6 is suggestive of left ventricular hypertrophy. (The peaks of the QRS complexes have been marked.)

Case 2. Female, aged 1 year. Admitted to hospital with acute pharyngitis and congestive heart failure. Dyspnœa on slightest exertion, recurrent respiratory infections and failure to thrive since 3 weeks of age. Never cyanosed. Increasing cardiac enlargement, pulmonary and hepatic congestion noted from 3 months of age. Radiological enlargement of both ventricles, pulmonary artery and hilar vessels with pulmonary congestion at 6 months of age (Fig. 4 and 5).

On examination at 1 year intense dyspnœa, underweight (13 lb.), prominent sternum, deep Harrison's sulci. Tachycardia 140 a minute. Moderate pulse pressure. Gross cardiac enlargement, heaving apex beat and variable parasternal, systolic thrill. Widespread, coarse, systolic murmur maximal up left sternal margin. Grossly accentuated pulmonary second sound. Crepitations throughout both lungs, bronchial breathing at left base.

Increase in cardiac enlargement on radioscopy and collapse of left lower lobe of lung. Cardiogram showed right and left ventricular hypertrophy (Fig. 6).

Death on first birthday. At necropsy gross cardiac enlargement (Fig. 7), both ventricles hypertrophied, left much more than right. Aorta larger than normal but pulmonary artery nearly twice its size. All valves competent. Defect through membranous ventricular septum with soft fibrous margins, measuring 1 cm. in its longest diameter and opening into the right ventricle beneath septal cusp of tricuspid valve.

Case 3. Male, aged 2½ years. Admitted for investigation. Recurrent respiratory infections since infancy, associated exertional dyspnœa.

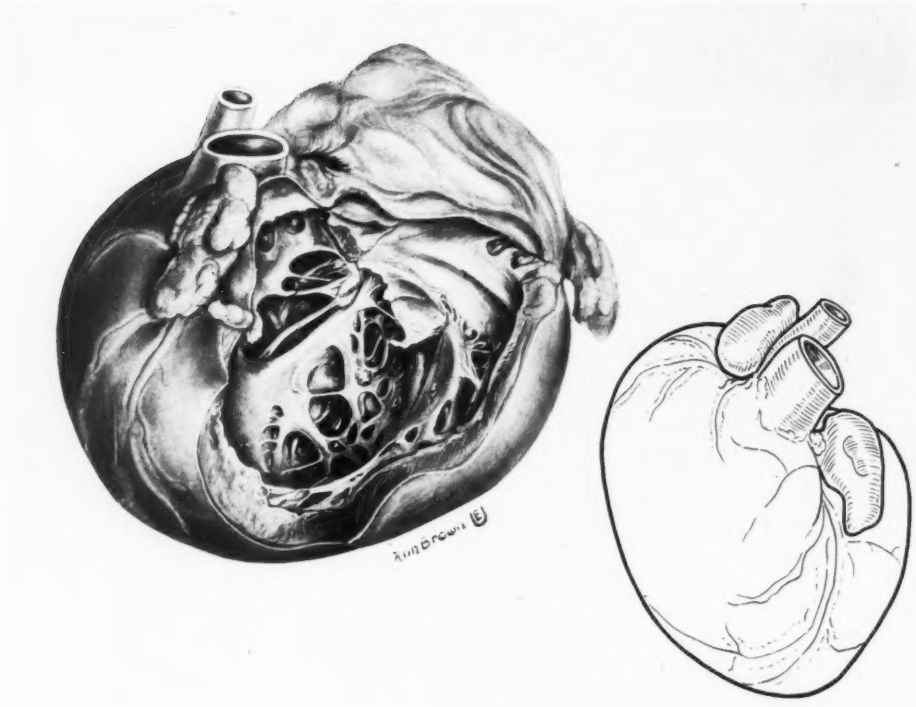

FIG. 3.—Drawing of heart from Case 1. Anterior cusp of mitral valve divided to show full extent of septal defect. Posterior wall of left atrium divided to show origin of aorta. Anterior rotation of left auricular appendage.

On examination, underweight (26½ lb.), deep Harrison's sulci and persistent tachycardia, 120 a minute. B.P. 102/70. No pulmonary or hepatic congestion. Marked cardiac enlargement. Systolic thrill down left sternal margin. Widespread, coarse, grating systolic murmur maximal in third interspace at left sternal margin. Pulmonary second sound accentuated.

On radioscopy considerable cardiac enlargement involving both ventricles (Fig. 8 and 9). Pulmonary artery enlarged and hilar vessels prominent. No hilar dance. Unusual cardiogram (Fig. 10) with left axis deviation but suggesting more hypertrophy of right than of left ventricle.

Clinical diagnosis was a large defect of the ventricular septum.

Case 4. Male, aged 13 months. Referred for investigation. Respiratory infection at 3 months of age. Subsequent recurrent episodes of pulmonary and hepatic congestion. Steady improvement with digitalis.

On examination grossly underweight (13 lb.) in spite of excellent home. Prominent sternum. Deep Harrison's sulci. Tachycardia, 140 a minute. B.P. 86/54. Marked cardiac enlargement but no pulmonary or hepatic congestion. Variable, parasternal, systolic thrill. Widespread, loud, very coarse, systolic murmur maximal in third interspace at left sternal margin. Variable, soft, diastolic murmur at lower end sternum and towards apex. Accentuated pulmonary second sound.

On radioscopy enlargement of both ventricles (Fig. 11 and 12). Slight left atrial enlargement; enlarged, pulsatile pulmonary artery and prominent, non-expansile hilar vessels. Cardiogram (Fig. 13) left axis deviation but suggesting hypertrophy of both ventricles in chest leads.

Clinical diagnosis was a large defect of ventricular septum.

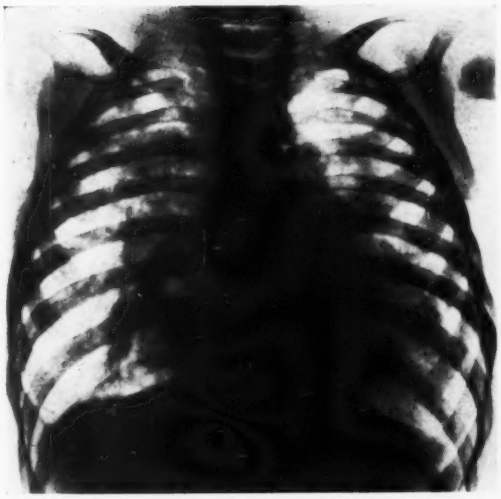

FIG. 4.—Radiograph (anterior) of Case 2 at 6 months. Generalized cardiac enlargement, enlarged pulmonary artery, prominent hilar vessels and pulmonary congestion.

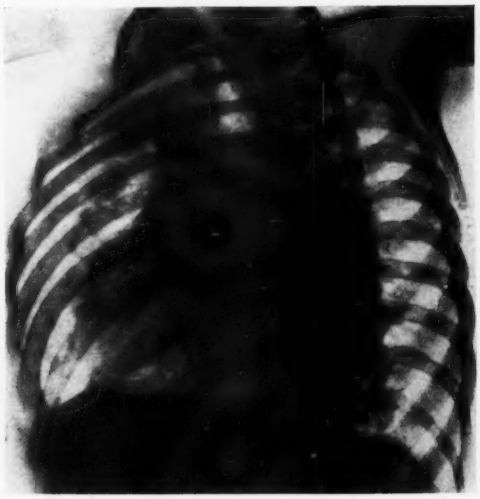

FIG. 5.—Radiograph (left anterior oblique) of Case 2 at 6 months. Enlargement of both ventricles.

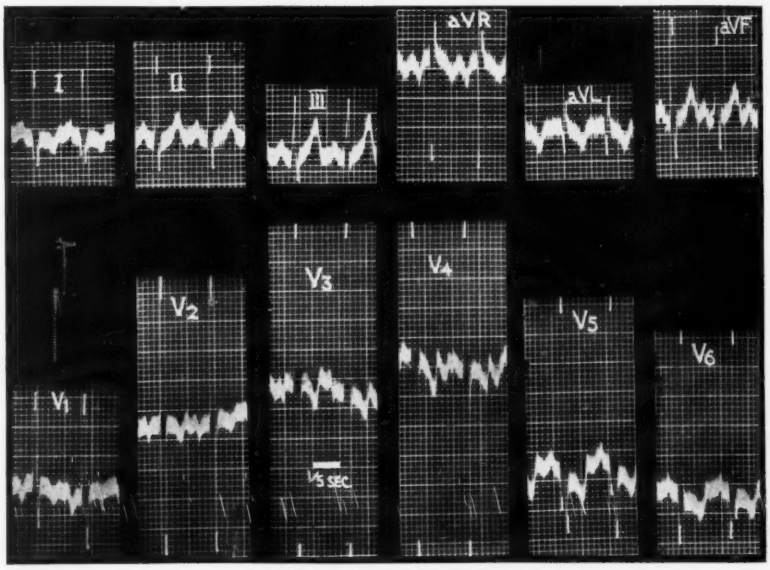

FIG. 6.—Electrocardiogram of Case 2 at 12 months. Tall R, moderate S and inverted T wave of right ventricular hypertrophy in V1; deep Q, tall R and inverted T of left ventricular hypertrophy in V6. (The peaks of the QRS complexes have been marked.)

FIG. 7.—Drawing of heart from Case 2. Defect replaces the membranous septum.

SUMMARY OF CASE NOTES

These four cases conform to a common clinical pattern of which the principal features are under-development of varying degree from an early age, an absence of cyanosis, a liability to respiratory infection, and a tendency to congestive heart failure in early childhood. There is gross cardiac enlargement, Roger's murmur, accentuation of the pulmonary second sound, and an occasional diastolic murmur down the left sternal margin. The pulse pressure tends to be small. Radiological examination shows the enlargement to involve both ventricles and the pulmonary artery. The hilar vessels are prominent. Electrocardiographic tracings suggest hypertrophy of both ventricles.

The main abnormality was a ventricular septal defect in Cases 1 and 2 and this was the clinical diagnosis in Cases 3 and 4. Although the actual malformations were very different in the first two cases, the clinical pictures were comparable.

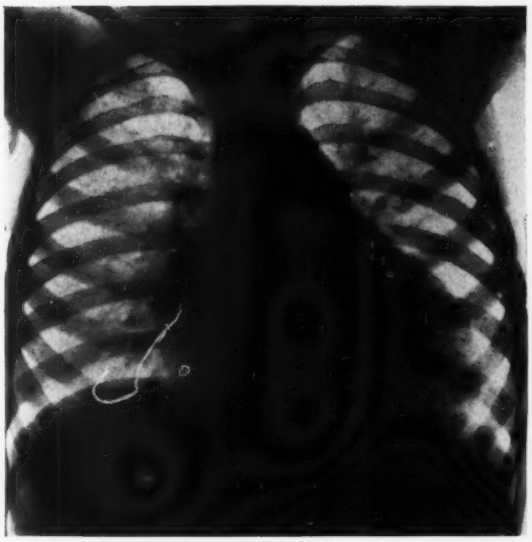

FIG. 8.—Radiograph (anterior) of Case 3 at two and a half years. Generalized cardiac enlargement, enlarged pulmonary artery and prominent hilar vessels.

FIG. 9.—Radiograph (left anterior oblique) of Case 3 at two and a half years. Enlargement of both ventricles.

DISCUSSION

Respiratory infection. The clinical picture in this small group of children is thus very different from the maladie de Roger in its classical form. Under-development and respiratory infections are rare in Roger's disease during the school period (Muir and Brown, 1934), but it is interesting that Roger (1879) thought that his cases, most of whom were young children, had a predisposition to respiratory disease. He thought, moreover, that such infection aggravated the disorder of the circulation. Müller (1920), 3 of whose 9 cases died under 2 years of age, also stressed the danger of pulmonary infection. Laubry and Pezzi (1921) have pointed out that the relatively symptomless ventricular septal defect represents an equilibrium between the ventricles which they consider is all too frequently broken. Although the circulatory dynamics of this concept require experimental confirmation, it is suggested that in early childhood a respiratory infection may be the factor that breaks this equilibrium and thus initiates a train of events, as illustrated by the four cases reported above, which may lead to congestive failure and death. Respiratory infection was responsible for the death of at least 10 of Abbott's 21 cases dying under 5 years of age. It was a major factor in at least 9 of the 28 cases in the Edinburgh Children's Hospital series.

All four cases showed deformity of the chest with well-marked Harrison's sulci. This is secondary to the recurrent respiratory infections and a weak chest musculature in early life (Naish and Wallis, 1948). Similar chest deformity has been observed in all types of congenital heart disease in which both these factors are present.

Subacute bacterial endocarditis. Bacterial endocarditis is a well-recognized danger in Roger's disease, but is uncommon in early childhood. Over the age of two years Gelfman and Levine (1942) report it as the cause of death in 8 out of 14 cases (57 %). Under that age they report it in only 2 out of 30 cases (7%). Of Abbott's 21 cases dying under five years of age bacterial endocarditis was the cause of death of only 2, and they were both over four years of age. None of the 28 cases in the Edinburgh Children's Hospital series showed evidence of bacterial endocarditis.

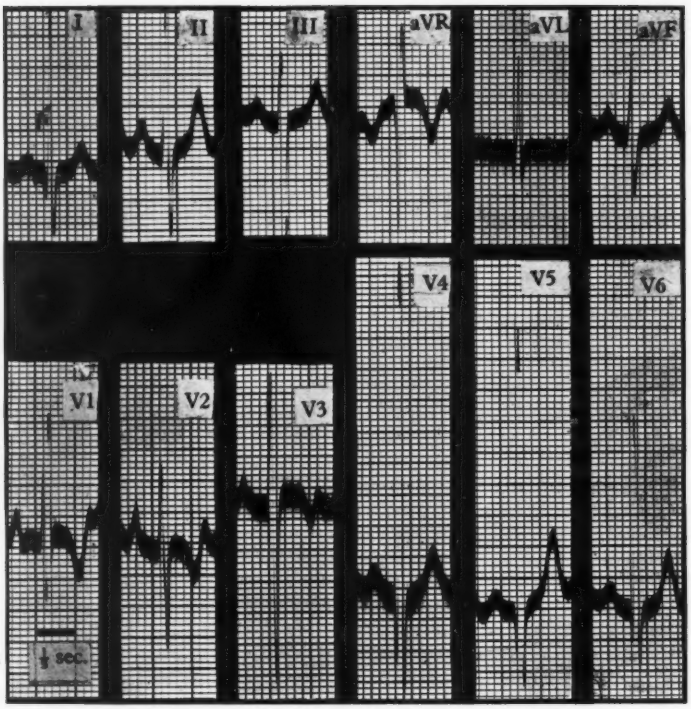

FIG. 10.—Electrocardiogram of Case 3 at two and a half years. Left axis deviation but deep S in lead I; R and R′ waves in V1 and height of R wave in aVR are suggestive of right ventricular hypertrophy; tall R wave in aVL and in V4 to V6 are suggestive of left ventricular hypertrophy.

Cardiovascular signs. In Roger's disease the shunt is small and there is little burden on the heart. The gross cardiac enlargement in the graver disability under discussion here is thought to be due to a greater flow of blood through the septal defect. This is especially liable to occur in the presence of associated anomalies such as aortic incompetence or when the defect is large. In spite of the increased volume of blood received by the right ventricle, the output of the two ventricles remains equal for the reason that the increased output of the right ventricle is passed through the lungs to the left side of the heart. The blood flow through the pulmonary artery is greater than that through the aorta as part of the left ventricular output forms the shunt to the right ventricle. There is thus an increased pulmonary blood flow, hypertrophy of both ventricles, enlargement of the pulmonary artery and relative depletion of the systemic circulation. As the pulmonary pressure rises, the right ventricle fails to clear its double intake and there is congestive failure with venous distension and liver engorgement.

The systolic murmur is no different from that described by Roger and there is no reason to suppose that it is not caused by the flow of blood through the defect. Accentuation of the pulmonary second sound was heard in all four cases. Such accentuation is a frequent finding in any lesion increasing the pressure in the pulmonary circulation. In older patients shown to have ventricular septal defects, catheterization of the pulmonary artery has demonstrated the increase of pressure in that vessel (Handelsman *et al.*, 1948; Griswold *et al.*, 1949; Burchell *et al.*, 1948). In Case 4 there was also a diastolic murmur at the lower end of the sternum. Similar murmurs

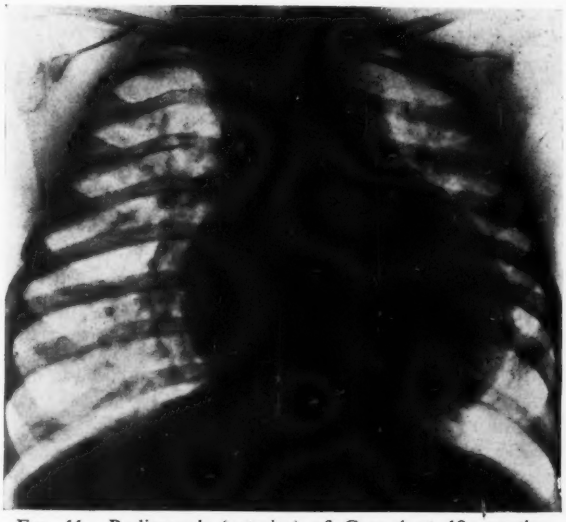

FIG 11.—Radiograph (anterior) of Case 4 at 10 months. Generalized cardiac enlargement and prominent hilar vessels.

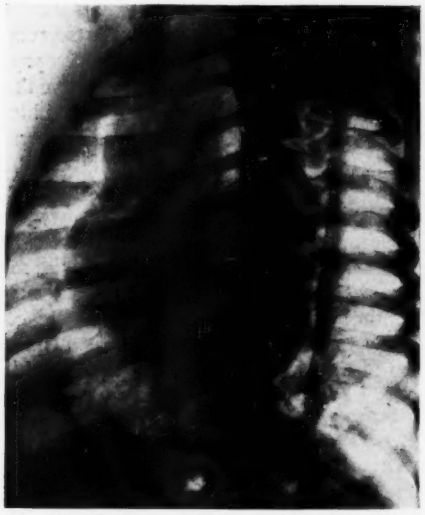

FIG. 12.—Radiograph (left anterior oblique) of Case 4 at 10 months. Enlargement of both ventricles.

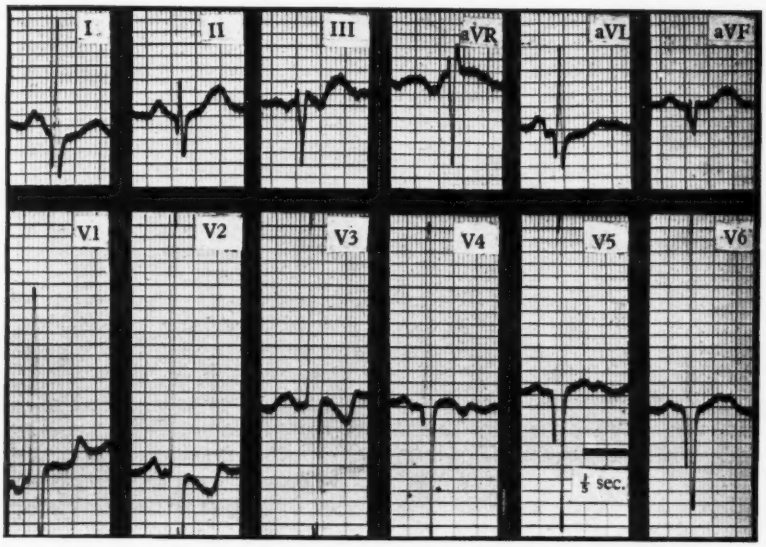

FIG. 13.—Electrocardiogram of Case 4 at 13 months. Left axis deviation but moderate S wave in lead I. Tall R wave in V1 is suggestive of right ventricular hypertrophy; deep Q, tall R waves in V5 and V6, and tall R wave in aVL are suggestive of left ventricular hypertrophy.

have been noted in older patients with Roger's disease, in patients shown on catheterization to have large defects of the ventricular septum (Baldwin, Moore, and Noble, 1946; Handelsman *et al.*, 1948), and in cases proved at necropsy to have isolated defects of the ventricular septum (Müller, 1920). This murmur is important in that its presence does not invalidate the diagnosis of ventricular septal defect. It is usually soft and blowing in character and best heard down the left sternal margin. Like the pulmonary second sound, it is thought to be due to the raised pulmonary pressure and thus similar to the Graham-Steell murmur in mitral stenosis. When one of the aortic cusps is involved in the defect, the diastolic murmur may be due to aortic incompetence (East, 1937).

Radiological and electrocardiographic features. In the young patient with Roger's disease radiological examination shows the cardiovascular shadow to be within normal limits. As age increases enlargement of both ventricles may become apparent and gross enlargement of the pulmonary artery has been seen. In such cases slight expansile pulsation may appear in the hilar shadows although it is never as obvious as that of the atrial septal defect. In contrast to this slowly developing picture, all four patients in this series showed enlargement of both ventricles and of the pulmonary artery from an early age. Although the hilar vessels were prominent, hilar dance was not seen in this age group.

The electrocardiogram is within normal limits until well on into adult life in the maladie de Roger. When changes do appear, they are those of left ventricular hypertrophy. This supports the contention that hypertrophy which increases the masses of both ventricles proportionately cannot be distinguished in the cardiogram from preponderant hypertrophy of the left ventricle (Wilson, Rosenbaum, and Johnston, 1947). In contrast, Case 2 showed cardiographic evidence of hypertrophy of both ventricles. This is all the more remarkable in that at autopsy the hypertrophy of the left ventricle was significantly greater than that of the right. In the other cases this double hypertrophy was not clearly shown in the unipolar chest leads. In the standard leads left axis deviation was usual, but the S wave tended to be prominent in lead I. In the unipolar chest leads a tall R was the main initial deflection in V1 and a tall R was preceded by a deep Q in V6. Although inconclusive, these changes are suggestive of hypertrophy of both ventricles.

Differential diagnosis. An atrial septal defect may be the cause of great cardiac enlargement and recurrent respiratory infections in early life (Taussig, 1947), but on clinical examination the signs are usually less marked than those of the cases reported here. Moreover, the enlargement is confined to the right side of the heart and the radiological contour is characteristic. The electrocardiogram is within normal limits or shows the changes of isolated right ventricular hypertrophy or of partial or complete right bundle branch block. It is not yet known how early or how frequently the pattern of right bundle branch block develops in childhood, but with increasing experience of unipolar cardiography it is considered that the cardiogram will be of even greater assistance in distinguishing the ventricular from the atrial septal defect.

Post-mortem figures suggest that the recurrent respiratory infections in the atrial septal defect do not impose such a heavy burden on the heart as they do in the ventricular septal defect. Of the 110 cases in the Edinburgh Children's Hospital series, only one had a significant defect of the atrial septum as an isolated lesion. This supports the experience of clinical practice in which it has been estimated that 82 per cent of cases of atrial septal defect are not recognized until the age of 20 years has been attained (Gilchrist, 1945).

A patent ductus arteriosus is only rarely of sufficient size to cause gross cardiac enlargement in early life. In such cases there may be difficulty in distinguishing the disorder from that of the group of children under discussion. This is especially so when the ventricular septal defect is associated with a diastolic murmur. One of Müller's (1920) cases who had been diagnosed clinically as a patent ductus was found post-mortem to have an isolated defect of the ventricular septum. When the ventricular septal defect is associated with aortic incompetence the pulse pressure is large and the differential diagnosis from a patent ductus may be extremely difficult (Laubry, Routier, and Soulié, 1933); but in the former the diastolic murmur tends to be maximal down the left sternal border, and when the ductus is of sufficient size to lead to early failure, a true Gibson murmur,

maximum below the inner third of the left clavicle, develops early. Radiologically prominence of the right ventricle in the left oblique view is uncommon in the patent ductus and the cardiogram is within normal limits or shows isolated left ventricular hypertrophy.

Prognosis. On the evidence of the four cases reported in this paper, the prognosis must be considered poor once this clinical picture has developed. Further experience may modify this view, but it is clear that the outlook does not compare with that of the classical form of Roger's disease.

It has been suggested that a ventricular septal defect, large and important in infancy, may, with the growth of the heart, become relatively smaller and of little consequence. The defect may ultimately become negligible and fail to give rise to physical signs (Brown 1939). The evidence for this is the disappearance of the systolic murmur and thrill as the child grows. The child is symptomless when the signs are present and remains so after their disappearance. It has not been suggested that a grossly disabled child later becomes symptomless. It is unlikely that such spontaneous closure of the defect can be hoped for in the clinical group described in this paper.

Summary

Necropsy reports show that the ventricular septal defect has a high mortality rate in early childhood. The cause of death in this age group is usually incidental disease. Respiratory infection is particularly dangerous.

Attention is directed to a group of children in whom a ventricular septal defect is directly responsible for death. The main pathological variations of the group are listed.

The clinical features of under-development, recurrent respiratory infections, early congestive heart failure, Roger's murmur, accentuation of the pulmonary second sound and an occasional diastolic murmur down the left sternal margin, represent the clinical picture of the ventricular septal defect in which the equilibrium between the ventricles has been broken in early childhood. It is suggested that this clinical picture is characteristic, irrespective of the factor responsible for the disturbance of equilibrium.

These views are supported by the clinical features in four cases, in the first two of which the presence of a ventricular septal defect was confirmed post-mortem.

The possible factors responsible for the development of the clinical features in this group are discussed and its differential diagnosis from the rarer cases of atrial septal defect and patent ductus arteriosus with disability in early life is considered.

The prognosis of the group appears to be poor.

Addendum

Since the completion of this paper, Soulié, Routier, and Bernal (1949) have again directed attention to the difficulty that may be experienced in differentiating a ventricular septal defect with associated aortic incompetence from a patent ductus arteriosus. Selzer (1949) has stressed the frequency of early diastolic murmurs in isolated defects of the ventricular septum.

I wish to express my thanks to Dr. A. Rae Gilchrist for much help and encouragement in the preparation of this paper and for permission to report Cases 3 and 4 ; to Prof. R. W. B. Ellis for permission to report Case 1; to Dr. J. L. Henderson for permission to report Case 2; to Dr. Agnes R. MacGregor for very helpful advice on the post-mortem specimens and for permission to go through the necropsy reports of the Royal Hospital for Sick Children, Edinburgh; and to Miss Ann Brown for her beautiful drawings.

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ATRIAL SEPTAL DEFECT

With special reference to the Electrocardiogram, the Pulmonary Artery Pressure and the Second Heart Sound

BY

J. M. BARBER, O. MAGIDSON, AND PAUL WOOD

From the Institute of Cardiology, London.

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The primary purpose of this paper is to present certain highly characteristic features of atrial septal defect that are either insufficiently well known or poorly understood: these include particularly the electrocardiographic appearances, the pressures in the right side of the heart, and the nature and significance of the second heart sound.

It is generally agreed that the diagnosis of atrial septal defect is based mainly on the radiological findings. These have been well described by Assmann (1928), by Roesler (1934), and by Bedford, Papp, and Parkinson (1941), and are now well recognized—at least in advanced cases. The right auricle, right ventricle, and main pulmonary artery are dilated; the left and right branches of the pulmonary artery are unusually large and dense, and may pulsate with great vigour, while heavy vascular shadows mark the lung fields. In contrast, the aorta and left ventricle are hypoplasic (Fig. 1 and 2).

McGinn and White (1933) and more recently Burrett and White (1945) agree with the authors cited above that a purely clinical diagnosis cannot be made with confidence, although certain features are suggestive: these include partial or complete arachnodactyly, relatively good health in childhood and adolescence, the frequent association of mitral valve disease, the rarity of bacterial endocarditis, the not infrequent occurrence of auricular fibrillation, a thrusting cardiac impulse associated with gross right ventricular dominance, a pulmonary systolic murmur often accompanied by a thrill, accentuation of the pulmonary second sound, a pulmonary diastolic murmur, and an audible third heart sound. Electrocardiograms in atrial septal defect may show tall P waves, slight prolongation of the P–R interval, right ventricular dominance or right bundle branch block (Bedford, Papp, and Parkinson, 1941). Historical details will be given more fully later.

In recent years cardiac catheterization has been used with increasing frequency to prove the diagnosis, samples of blood obtained from the pulmonary artery, right ventricle, and right auricle containing appreciably more oxygen than samples from the venæ cavæ (Howarth *et al.*, 1947).

Angiocardiography has proved less helpful, for the shunt is normally from left to right auricle, and the contrast medium becomes so diluted that it does not show up well after returning to the left auricle from the lungs. It is true that diodone may pass through the defect from right to left, owing to the high pressure generated in the right auricle by the force of the injection, but this does not distinguish atrial septal defect from patent foramen ovale.

Cases Used for Present Study

A series of 62 cases of atrial septal defect is presented. The electrocardiograms from 3 additional cases are considered. The diagnosis depended primarily upon the radiological features, but was confirmed in 21 by cardiac catheterization. No patient with persistent central cyanosis, advanced

FIG. 1.—Skiagram of a case of atrial septal defect in a boy, aged 12, with gross enlargement of the pulmonary artery and its branches.

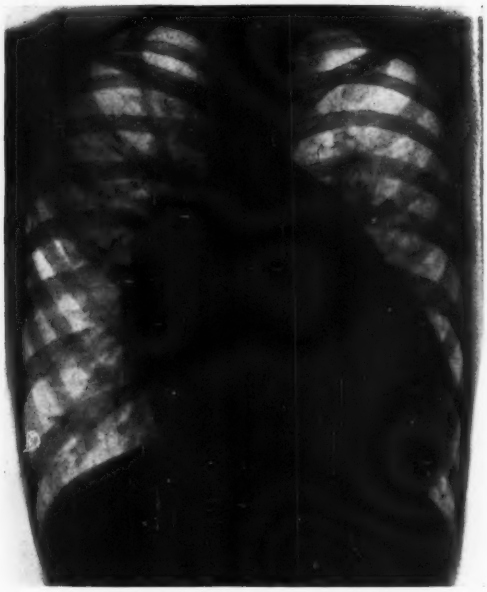

FIG. 2.—Skiagram of a case of *A.S.D.* in a girl, aged 7, showing gross enlargement of the heart shadow and marked engorgement of the pulmonary vascular tree (pulmonary plethora).

emphysema, or obvious mitral stenosis with dilatation of the left auricle was included. Care was also taken to exclude primary pulmonary hypertension, idiopathic dilatation of the pulmonary artery, simple pulmonary valvular stenosis, ventricular septal defect, and patent ductus—if necessary by cardiac catheterization.

CLINICAL FEATURES

Age and sex. The distribution of cases over the various age groups is shown in Table I. The youngest patient was aged 5 years, the eldest 66 years. The high incidence of patients over 30 (53%) is a unique feature of this form of congenital heart disease, and has been noted by all observers.

TABLE I

AGE INCIDENCE IN 62 CLINICAL CASES OF *A.S.D.*

0–10 years of age	5 cases
11–20 ,, ,,	14 ,,
21–30 ,, ,,	10 ,,
31–40 ,, ,,	13 ,,
41–50 ,, ,,	11 ,,
51–60 ,, ,,	6 ,,
61–70 ,, ,,	3 ,,

The preponderance of women is also well known, the ratio of females to males being 4 : 1 in the necropsy series reported by Bedford, Papp, and Parkinson (1941) and 3 : 2 in Roesler's series. In our 62 cases there were 43 females and 19 males, a ratio of over 2 : 1.

Symptoms and signs. The majority of patients were breathless on exertion (Table II) and seven,

all over 40 years of age, had congestive heart failure. None had hæmoptysis. Of 13 cases entirely free from symptoms, 6 were vigorous school children under 16 years of age, 3 were active young women aged 22, 29, and 31, 3 were boys aged 16, 16, and 19, and the thirteenth was a male clerk aged 52. The physical signs are recorded in Table II.

TABLE II

CLINICAL FEATURES OF 62 CASES

No symptoms	13	Apex beat:	
Dyspnœa on exertion	41	Displaced to the left	28
Left inframammary pain	4	Impalpable	3
Palpitation	5	Tapping or forcible	41
Hæmoptysis	0	Normal quality	9
" Faints " or faintness	4	Systolic thrill	22
		Present or maximal at pulmonary area	16
Congestive heart failure	7	Systolic murmur	62
		Heard in pulmonary area	52
Hypertension	6	Pulmonary diastolic murmur	36
Cyanosis (all in congestive heart failure)	3	Mitral diastolic murmur	9
Clubbing of fingers	0	Basal second sound widely split (grade 3)	52
		Basal second sound loud	27
		Audible third heart sound	26

Appearance. Under-development, frailness, the gracile habitus, arachnodactyly, high arched palate, and præcordial bulge have all been described as characteristic. One or more of these features were observed in a number of our cases, especially high arched palate and pigeon chest; but as their absence was rarely recorded in the notes, we are unable to tabulate their incidence.

Blood pressure. This was usually normal, but was raised in 6 cases, 2 of which had congestive heart failure.

Pulse. The rhythm was regular in 55 patients: auricular fibrillation occurred in six (aged 43–62), five of whom had congestive heart failure; flutter was recorded in one (aged 63) also in failure. Three of those with auricular fibrillation had a mitral diastolic murmur. The pulse was noticeably small in many, but was often normal.

Cyanosis. Cyanosis was observed in three patients, all of whom had congestive failure. In one of them the arterial oxygen saturation fell to 70 per cent on one occasion. There was no instance of clubbing of the fingers.

Cardiac impulse. It was Roesler (1934) who first emphasized the fact that a well circumscribed powerful thrust at the apex beat in the presence of gross right ventricular dominance was not only characteristic of atrial septal defect, but occurred in no other condition. We observed this type of cardiac impulse in several of our cases, and have come to regard it as evidence of a hyperkinetic right ventricle—a vigorously acting chamber with a greatly increased stroke volume. We prefer to describe it as tumultuous, to distinguish it from the tap of mitral stenosis, from the sustained heave of left ventricular hypertrophy, and from the sharp thrust of thyrotoxicosis. It is not unlike the cardiac impulse in patent ductus (due to similar behaviour of the left ventricle) and probably very like that in pure beri-beri (Wenckebach, 1928). The most impressive example occurred in a man who was subsequently found to have a heart weighing 940 g., enlargement being entirely right-sided. In two-thirds of our cases, however, the cardiac impulse was tapping.

The apex beat was usually displaced beyond the mid-clavicular line, and occasionally beyond the anterior axillary line.

Thrills. A systolic thrill was recorded over the outflow tract of the right ventricle in 16 cases, but could not always be detected at every examination. Occasionally, a systolic thrill was confined to the apex—possibly due to associated mitral valve disease.

Heart Sounds

Particular attention was paid to the second heart sound: it was widely split in 52 cases and noticeably accentuated in 27 cases.

It is usually stated that accentuation and splitting of the pulmonary second sound is evidence of pulmonary hypertension. We feel that this belief needs revision. In the first place it is rarely possible to recognize a pulmonary or aortic second sound, but only a second heart sound. It is reasonable to assume that the major part of it is normally aortic, because the aortic pressure is so much higher than the pulmonary. Thus in certain cases of aortic stenosis, the second heart sound may be almost inaudible, whereas in Fallot's tetralogy it is frequently quite loud, though single: the aortic element is absent from the first, the pulmonary from the second.

We have made a special study of the second heart sound in children and adults of all ages. Some degree of splitting can be detected clinically in most normal subjects; there were no exceptions in 100 children examined, and few in adults.

Three grades of splitting may be recognized: in grade I two elements can only just be appreciated, and an inexperienced observer may not perceive more than one; in grade II the split cannot be doubted, but the elements are still close; in grade III there is conspicuous wide splitting which is certainly pathological. Splitting in normal children is usually grade II, in normal adults grades I or II. In atrial septal defect it is commonly grade III. In right bundle branch block it is also grade III.

Conditions that might be expected to cause slight delay in aortic valve closure, such as hypertension, may be associated with a single or almost single second heart sound, and splitting in left bundle branch block may be only grade I. On the other hand grade II splitting is common in mitral stenosis, and grade III splitting in any circumstances usually means right bundle branch block. This suggests that the aortic element normally precedes the pulmonary element, despite electrokymographic evidence that the right ventricle begins to contract before the left (Luisada and Fleischner, 1947).

TABLE III

AGE OF PATIENTS WITH *A.S.D.* AND A LOUD THIRD HEART SOUND

Age in years	No. of cases with loud third heart sound	Total cases
0–10	1	5
11–20	7	14
21–30	4	10
31–40	4	13
41–50	5	11
51–60	2	6
61–70	3	3
	26	62

The intensity of the second heart sound requires separate analysis. Accentuation may be due to increased intensity of either element, and it is only possible to tell which element when there is sufficiently wide splitting; however, the answer can usually be determined indirectly by considering the clinical circumstances. The intensity of the sounds appears to depend upon the pressures in the aorta and pulmonary artery, and upon the relationship of the pulmonary artery to the anterior chest wall.

In atrial septal defect the mean pressure in the right ventricle and pulmonary artery may be normal or little above normal in the presence of grade III splitting. It is therefore reasonable to attribute the split to right bundle branch block or to delay in the emptying time of an over-filled right ventricle. Increased intensity of the second element, when present, may be due to the proximity of the dilated pulmonary artery to the chest wall. An extremely loud pulmonary element, however, usually means pulmonary hypertension and does not favour *A.S.D.*

A third sound best heard at the apex or lower end of the sternum was noted in 26 instances. In 14 of these the patient was over the age of 30 years, and in 5 there was associated mitral stenosis (without dilatation of the left auricle). The incidence of the third heart sound in relation to the age of the patient is presented in Table III.

Murmurs. No case was seen without a cardiac murmur. A *systolic* murmur was heard in all, and was maximal over the pulmonary artery in 52 of them. An *early diastolic* murmur was heard down the left border of the sternum in 36 cases (Table IV). It was usually short and rather high pitched, and might only be heard on careful auscultation in a quiet room. Although presumably due to pulmonary incompetence, the murmur was not confined to cases with gross cardiac enlargement or to those with very large pulmonary arteries, but was noted as frequently in young patients with relatively slight radiological changes in whom the diagnosis was established with certainty only by means of cardiac catheterization. It is therefore regarded as an important sign of *A.S.D.*

A rumbling presystolic or mid-diastolic murmur was heard at the apex in 9 instances and was attributed to mitral stenosis (Lutembacher's syndrome). As previously stated, such cases were only included when there was no other evidence of mitral stenosis. In distinguishing clinically between *A.S.D.* and other anomalies resulting in an increased pulmonary blood flow, a mitral diastolic murmur does not help, for it is a common expression of turbulence at the mitral orifice in both patent ductus and ventricular septal defect. If the murmur is ever functional in *A.S.D.* it must arise at the site of the defect, not at the mitral valve, for the mitral blood flow is diminished rather than increased, and the left ventricle tends to be underfilled.

TABLE IV

AGE OF PATIENTS WITH *A.S.D.* AND A PULMONARY DIASTOLIC MURMUR

Age in years	No. of cases with pulmonary diastolic murmur	Total cases
0–10	3	5
11–20	10	14
21–30	6	10
31–40	8	13
41–50	3	11
51–60	3	6
61–70	3	3
	36	62

Cardiac failure. Cardiac failure was seen in seven patients, all of whom were over 40 years of age (Table V). Five of them had auricular fibrillation, one had auricular flutter, and one normal sinus rhythm; while three presented clinical evidence of mitral stenosis. Reversal of the interatrial shunt, causing central cyanosis, was observed once (Case 30) with an arterial oxygen saturation of 70 per cent. Two other cases were cyanosed, but were not specially investigated in this respect.

TABLE V

AGE OF CASES OF *A.S.D.* WITH CONGESTIVE HEART FAILURE

(At time of first admission with failure)

Case 44	43 years of age
Case 30	47 ,, ,,
Case 46	48 ,, ,,
Case 4	49 ,, ,,
Case 8	50 ,, ,,
Case 43	62 ,, ,,
Case 42	63 ,, ,,

All the patients admitted with congestive heart failure, except one who died suddenly (Case 44), responded satisfactorily to the usual methods of treatment.

Cardiac Catheterization in Atrial Septal Defect

Venous catheterization of the heart as an aid to the diagnosis of congenital heart disease is now an accepted and widely practised procedure. Its use in the diagnosis of *A.S.D.* has been mentioned by a number of authors, including Brannon *et al.* (1945), Dexter *et al.* (1947 *a*, *b*, *c*), Sosman *et al.* (1947), Howarth *et al.* (1947), and Bing *et al.* (1948).

Passage of a catheter from right to left auricle does not distinguish *A.S.D.* from patent foramen ovale; it is necessary to demonstrate an interatrial shunt from left to right. This is achieved by showing that samples of blood from the right auricle, right ventricle, and pulmonary artery are similar and contain appreciably more oxygen than samples from the venæ cavæ. The volume of the shunt may be calculated by subtracting the systemic blood flow from the pulmonary blood flow.

In this series the diagnosis of *A.S.D.* was confirmed by catheterization in twenty-one instances (Table VI). Samples from the chambers on the right side of the heart (R.A., R.V., and P.A.) were similar and showed an average oxygen unsaturation of 31 ml. per litre, compared with 62 ml. per litre in the superior vena cava. The difference was always well beyond the margin of technical error. Samples obtained from the left side of the heart in six instances were between 92 and 95 per cent saturated.

TABLE VI

Results of Cardiac Catheterization

Case	Sex	Age	Oxygen unsaturation ml/litre				Mean pressure in cm. saline above sternal angle		
			S.V.C.	R.A.	R.V.	P.A.	R.A.	R.V.	P.A.
C. ..	M.	17	60	33	30	—	−1	+16	—
D.B. ..	F.	22	66	28	40	—	—	—	—
J.I. ..	F.	12	55	40	37	—	+5	+19	—
Mrs. D. ..	F.	35	45	30	31	28	−3	+6	+8
G.F. ..	M.	16	56	25	23	17	+1	+14	+19
A.W. ..	F.	18	68	28	28	27	±0	+14	+18
J.D. ..	F.	18	63	38	31	36	−1	+15	+22
U.M. ..	F.	34	72	32	26	30	−2	+16	+22
I.M. ..	F.	21	70	34	—	—	—	—	—
F.K. ..	M.	25	56	26	—	—	—	—	—
F.Mc. ..	F.	25	68	35	33	—	−1	+20	—
E.H. ..	F.	36	75	35	33	—	±0	+15	—
S.H. ..	F.	16	67	29	29	—	—	+9	—
J.H. ..	F.	51	70	32	30	—	+7	+19	—
M.Mc. ..	F.	25	75	56	60	60	−4	+15	+11
P.H. ..	F.	12	64	—	40	—	—	+20	+18
C.O. ..	F.	31	55	35	—	—	+6	—	—
B.T. ..	F.	6½	62	40	—	—	±0	—	+16
G.C. ..	M.	5	42	20	18	—	+2	+12	—
M.L. ..	F.	14	43	28	17	16	+1	+10	+10
F.D. ..	M.	29	60	25	16	—	−4	+8	—

Mean pressures in the right ventricle and pulmonary artery were but little raised, the range being 6–20 cm. of saline (4–15 mm. Hg.) in the right ventricle and 8–22 cm. of saline (6–16 mm. Hg.) in the pulmonary artery. The right auricular pressure was usually normal, but was raised in three instances.

The mean left auricular pressure, when obtained, was a little higher than the right, but rather less so than in controls with patent foramen ovale. The mean left ventricular pressure was between 48 and 72 cm. of saline (35–53 mm. Hg.) in the 5 cases in which this chamber was entered.

Simple calculations indicate that the pulmonary blood flow in *A.S.D.* averages about two and a half times the systemic flow, and is of the order of 10 litres a minute; thus the amount of blood shunted back to the right auricle is usually greater than the volume passed forwards to the left ventricle. The systemic flow is either normal or slightly reduced.

The Electrocardiogram

The value of the electrocardiogram in *A.S.D.* has received increasing emphasis since Roesler's (1934) review. He had available only 7 electrocardiographic records from 62 cases. He noted right axis deviation, moderate in 4 cases and marked in 1, and stated that enormous dilatation of the right ventricle with moderate hypertrophy does not cause a high degree of right axis deviation. Leech (1935) described high P waves with or without slight right ventricular preponderance. Bedford and Brown (1937) found right axis deviation often with inverted T waves in leads II and III and sometimes a widened QRS complex suggesting bundle branch block. Routier and de Balzac (1938) and Routier *et al.* (1940) stressed the diagnostic significance of the electrocardiogram ; of 300 cases of congenital heart disease the standard limb leads showed right bundle branch block (right *B.B.Bl.*) in 23; of these 20 proved to be cases of *A.S.D.*

Schnitker (1940) in his monograph considered that the absence of right axis deviation was no bar to the diagnosis of *A.S.D.*; " definite right ventricular preponderance " was seen in only 3 of 9 cases. He also commented on large P waves, occasional auricular fibrillation or flutter, abnormal notching of the QRS complex, and biphasic QRS complexes which Katz and Wachtel (1937) have described as pathognomonic of congenital heart disease.

Bedford, Papp, and Parkinson (1941) studied the electrocardiogram in detail in their series of 53 cases. They found auricular fibrillation in 6 (5 with mitral stenosis) and flutter in 1. Large high P waves in one or more leads were seen in 15 cases; the auricular complex was large and bifid in three instances that were proved not to have mitral stenosis. They drew attention for the first time to the prolonged P–R interval. In 19 cases it was 0·20 seconds or more and in one instance with partial right *B.B.Bl.* it was 0·28 seconds. Right axis deviation occurred in 41 and left axis deviation in 2 cases. There were 5 records showing right *B.B.Bl.*, and 21 with a widened ventricular complex sometimes suggesting right *B.B.Bl.* This type of graph was seen only twice in patients below the age of 30 and then with moderate cardiac enlargement. In one case right *B.B.Bl.* was seen to develop after 4 years observation. The authors were thus forced to agree with Routier *et al.* (1940), that right *B.B.Bl.* was not an integral part of the congenital lesion but a sequel to it, and was closely related to right ventricular dilatation.

Burrett and White (1945) found right axis deviation, moderate or marked, in a high percentage and considered this very helpful in diagnosis. Taussig (1947) states that the electrocardiogram shows high P waves, frequently a prolonged P–R interval, and not uncommonly widening and notching of the QRS complex. Right axis deviation is in her opinion the rule, but is not marked, because enlargement of the right ventricle is a combination of dilatation and hypertrophy.

Dry (1948) interpreted the electrocardiographic findings as indicating right ventricular strain, and noted impaired intraventricular conduction in 3 of his 5 cases. One of those with right *B.B.Bl.* was only 9 years old, and the author offered this as evidence against the view that the conduction defect was a sequel to, rather than a part of, the congenital lesion.

In the present series the initial electrocardiogram consisted of leads I, II, III, aVR, aVL, aVF, and V1, V3, and V5. About one-third of the cases also had leads from the right chest, V3R and V5R, and from the xiphisternum, VE (Wilson). All records were taken with the patient recumbent. The electrical axis was measured in the standard limb leads by the method of Carter *et al.* (1919). Axes between 0 and 90 were classed as normal. The electrocardiographic data so obtained in 65 cases are presented in Table VII.

P wave. Conspicuous pulmonary or mitral P waves were not a feature of the *A.S.D.* electrocardiogram; thus, only two cases showed auricular complexes exceeding 2·5 mm. in height, and in the majority of records the P waves were within normal limits. This point has not been sufficiently appreciated.

P–R interval. There was a strong tendency for the P–R interval to range around the upper limit of normal and in eleven cases it exceeded 0·22 seconds.

Electrical axis. Well marked left axis deviation was seen in 8 cases, but all had right *B.B.Bl.*

TABLE VII

ELECTROCARDIOGRAPHIC DATA IN 65 CASES OF *A.S.D.*

Electrical axis		
Right axis deviation	39	
Normal	18	
Left axis deviation	8	
P wave		
Height greater than 2·5 cm. in lead II	2	
2·0 to 2·49 mm. in lead II	21	
Width of P in lead II greater than 0·11 seconds	11	
P–R interval		
0·20 to 0·22 seconds	25	
0·23 to 0·25 seconds	5	
0·26 and more (4 cases 0·26, 2 cases 0·28)	6	
Right *B.B.Bl.*		
0·12 seconds or greater	24	95%
0·09 to 0·11 seconds	38	95%
Right ventricular hypertrophy pattern without right *B.B.Bl.*	3	
Height of R′ in lead V1 in right *B.B.Bl.*		
Over 15 mm.	3	
10 to 14·9 mm.	5	
5 to 9·9 mm.	37	
Auricular fibrillation (patients aged 43, 48, 49, 50, 51, 59, 62 years)	7	
Auricular flutter (age of patient 63 years)	1	
Normal sinus rhythm	57	

Similar curves were described by Bedford *et al.* (1941). Left axis shift was brought about in one of two ways. In 2 cases the heart was electrically vertical and deep S waves in lead V6 were transmitted to the left leg, and hence to standard lead III (Fig. 3). In the others the heart was semi-horizontal with a shallow S wave in leads from the left præcordium (Fig. 4); like Soulie and Joly (1948) we noted that in some of these cases VL and VF did not reflect unequivocal left or right ventricular potentials, and we were thus unable to determine the electrical position of the heart.

Right ventricular hypertrophy. There were only 3 cases with electrocardiograms showing dominant R waves without widening or notching in lead V1 (Fig. 5). These patients were young (aged 9, 12, and 16) and had little cardiac enlargement. In two the diagnosis of *A.S.D.* was confirmed by means of cardiac catheterization. It is certainly possible that right *B.B.Bl.* may develop later in these cases, as the right ventricle enlarges. On the other hand, like Dry (1948), we have 8 cases showing right *B.B.Bl.* in childhood (aged 5, 6, 7, 8, 11, 11, 12, and 13 years). Moreover, two of those with simple right ventricular dominance showed notching of the R wave in lead V1 followed by an S wave. This may represent impaired conduction in the wall of the right ventricle.

Height of R′ in lead V I. Wilson *et al.* (1947) state that conspicuous hypertrophy of the right ventricle combined with right *B.B.Bl.* greatly increased the voltage of the secondary R wave (R′) in leads from the right præcordium. It will be noted from Table VIII that the height of R′ in lead V I varied considerably in this series, and we could not correlate it with the size of the right ventricle. In several patients with considerable right ventricular enlargement the amplitude of R′ was only 2–3 mm. On the other hand, when right *B.B.Bl.* is associated with pulmonary hypertension (and presumptive right ventricular hypertrophy) we agree that tall secondary R waves are the rule (Fig. 6).

Right bundle branch block. The most significant electrocardiographic feature of this series was the remarkably high incidence of the right *B.B.Bl.* pattern: this occurred in 62 cases, or in 95 per cent. Multiple V leads undoubtedly aided its recognition. According to the criteria of Wilson *et al.* (1947), 38 of these cases had incomplete right *B.B.Bl.* (Fig. 7), QRS measuring only 0·09 to

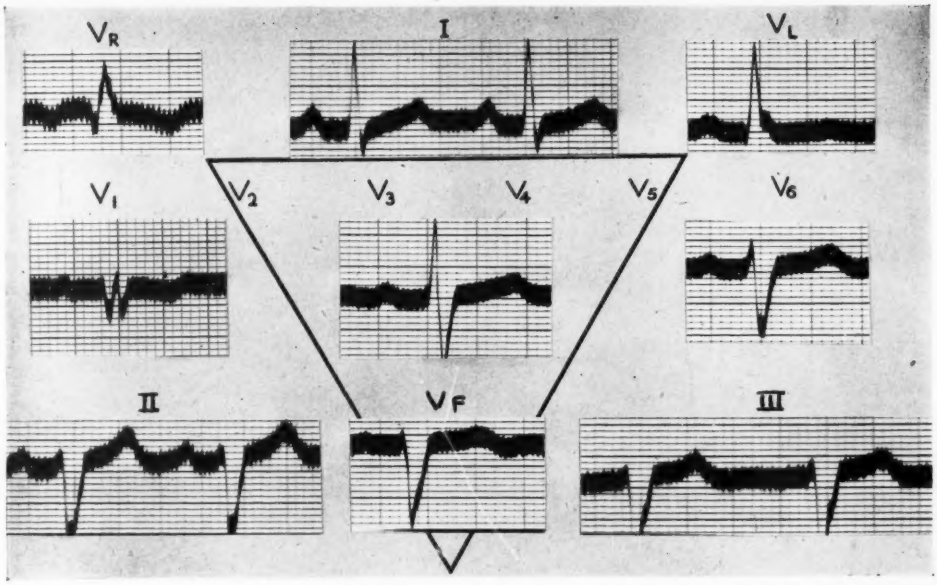

FIG. 3.—Electrocardiogram in a case of *A.S.D.*, showing left axis deviation with right *B.B.Bl.* The heart is vertical, the left ventricular surface pattern seen in V6 being conducted to the left leg (VF).

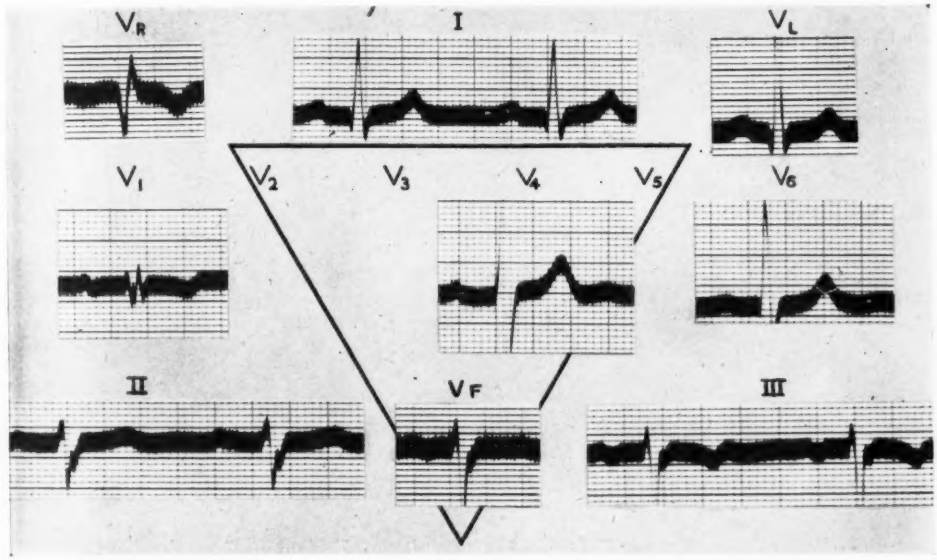

FIG. 4.—Electrocardiogram in a case of *A.S.D.*, showing left axis deviation with right *B.B.Bl.* The electrical position of the heart is horizontal. The deep S wave in lead VF (and hence in leads II and III) is probably derived from lead V2 or V3.

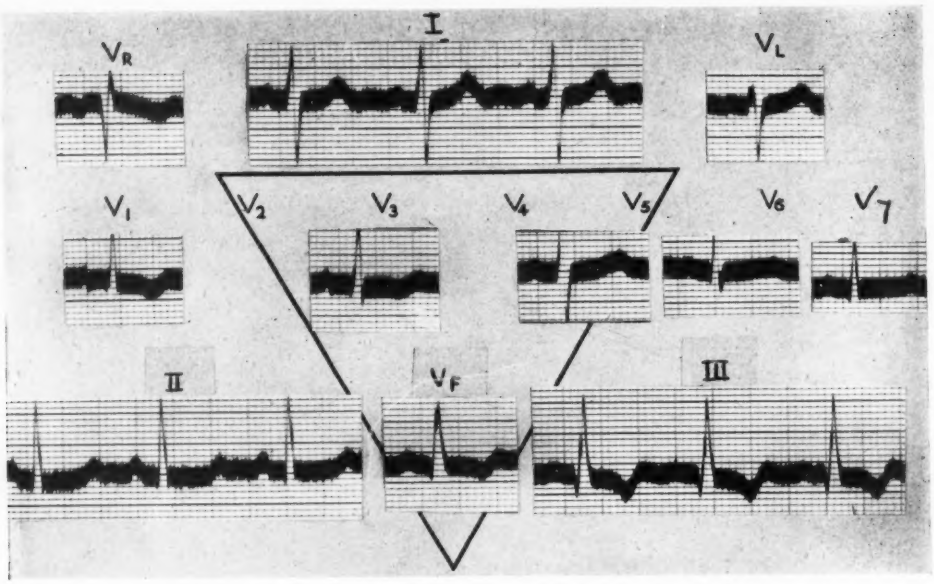

FIG. 5.—Electrocardiogram in a case of *A.S.D.*, showing right ventricular dominance with no evidence of right *B.B.Bl.*

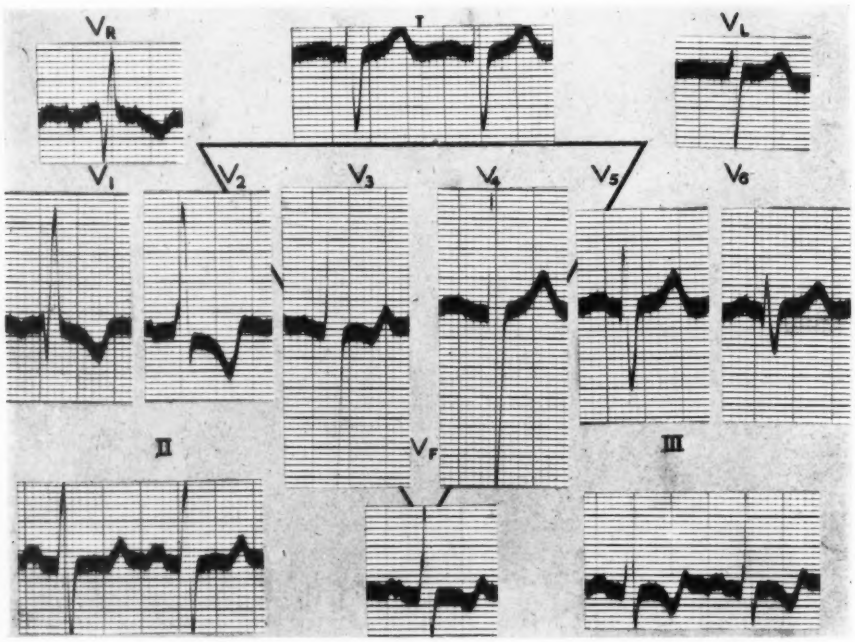

FIG. 6.—Electrocardiogram in a case of pulmonary hypertension with right *B.B.Bl.*, showing an unusually tall secondary R wave in leads V1 and V2.

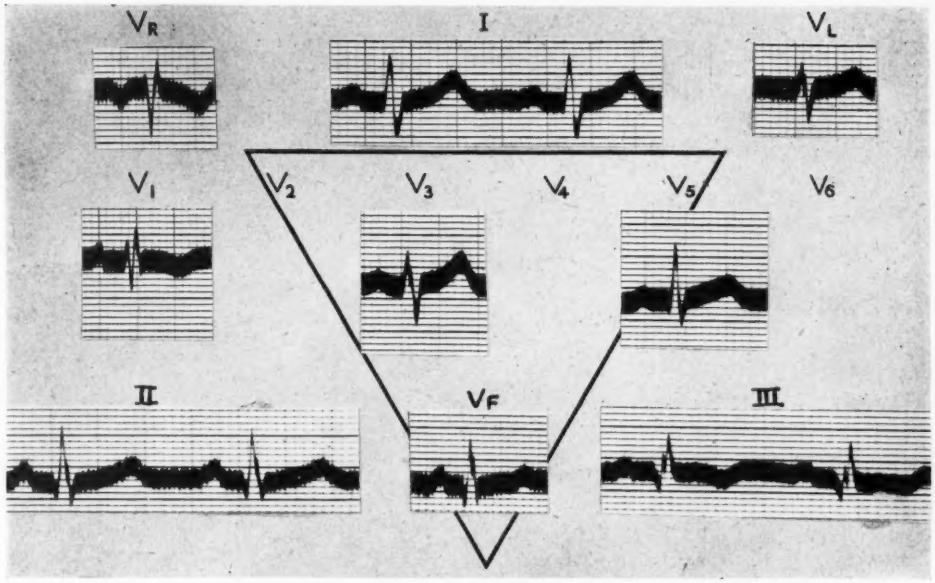

FIG. 7.—Electrocardiogram from a case of *A.S.D.*, showing partial right *B.B.Bl.*

0·11 seconds, and there being a deep or wide S wave in left ventricular surface leads or their counterparts (usually VL and standards lead I). The limb leads were rarely diagnostic. We relied mainly on finding a conspicuous secondary R wave (R′) in leads VI and VE, associated with slight or moderate widening of QRS (Fig. 8). The secondary R wave was often quite small in height and sometimes measured only 2 mm. Occasionally it was followed by a small secondary S wave (S′), but this was never seen in lead V3R. In the majority of cases R′ also occurred in lead V2 and often in lead V3 (Fig. 9). It is admitted that a small secondary R wave may occur in lead V I in normal children and occasionally even in normal adults, but it is inconspicuous and QRS is not widened.

The right arm lead VR showed a QR complex with an inverted T wave in the majority; in a few there was a small initial positive deflection giving an RSR′ complex.

The diagnostic importance of partial or complete right *B.B.Bl.* is further emphasized by its relative infrequency in mitral stenosis (6%), tetralogy of Fallot (10%), simple pulmonary stenosis (20%), and pulmonary heart disease (4%). The details of this comparative study are given in Table VIII.

TABLE VIII

VENTRICULAR COMPLEXES IN OTHER CONDITIONS AFFECTING THE RIGHT SIDE OF THE HEART

	Mitral stenosis	Tetralogy of Fallot	Pulmonary stenosis	Chronic pulmonary heart disease
Number of cases	64	33	10	100
Ventricular complexes normal	51	0	3	—
Right ventricular hypertrophy	9	30	5	—
Right bundle branch block	4	3	2	—
Percentage with right *B.B.Bl.*	6	10	20	4

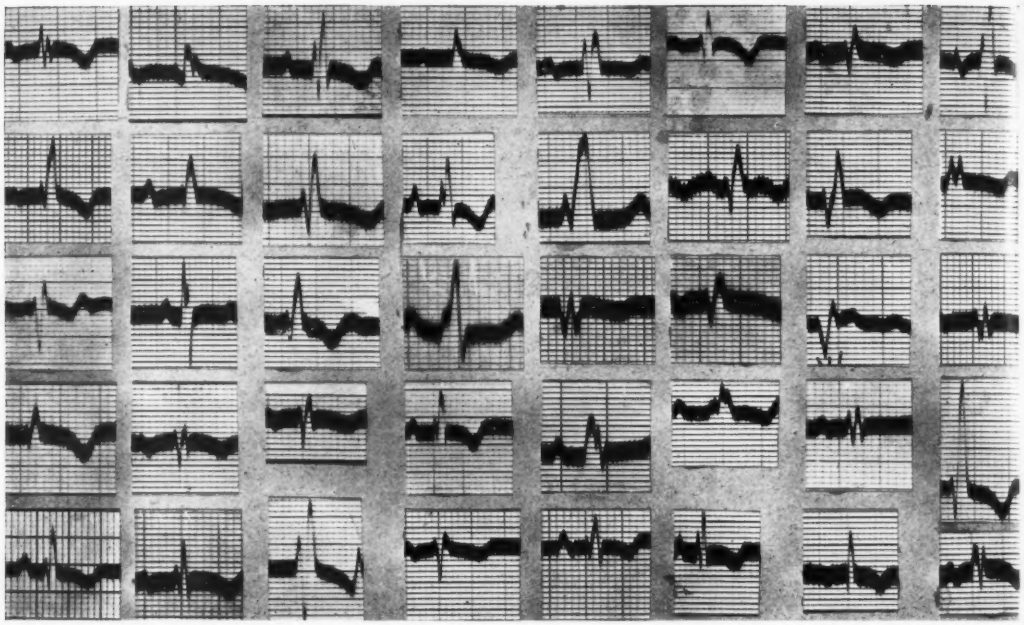

FIG. 8.—Electrocardiograms from lead V1 in 40 unselected cases of *A.S.D.* Nearly all show partial or complete right *B.B.Bl.*

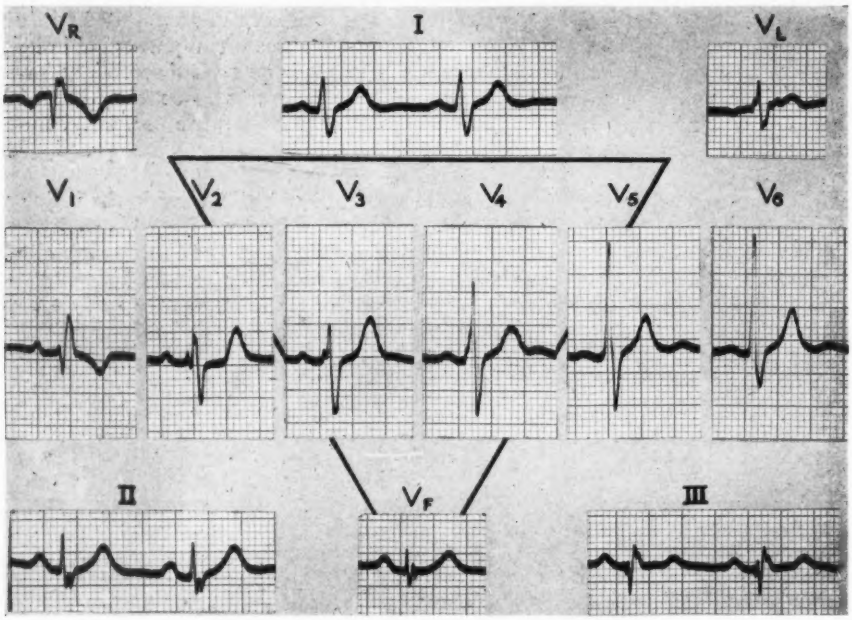

FIG. 9.—Typical example of right *B.B.Bl.* in a case of *A.S.D.*

Discussion

Atrial septal defect is now widely recognized as the commonest single congenital cardiac anomaly and as one compatible with many years of active life. Its distinction from other forms of congenital heart disease is particularly important, because *A.S.D.* alone requires no protection from bacterial infection, and penicillin need not be given every time the patient has a sore throat or dental attention. Moreover, the rapid advance of cardiac surgery gives rise to some hope that *A.S.D.* may be repaired before long (Murray, 1948).

It is urged that a clinical diagnosis should be made with more confidence, the combination of a small or normal pulse, tapping or tumultuous cardiac impulse, lifting right ventricular outflow tract, pulmonary systolic murmur (with or without a thrill), pulmonary diastolic murmur, and widely split second heart sound in an acyanotic child or adult being practically diagnostic. Marked accentuation of the pulmonary element of the second heart sound favours pulmonary hypertension rather than *A.S.D.* As stated earlier in the paper, the presence of a mitral diastolic murmur does not favour *A.S.D.* (as Lutembacher's syndrome), for it is even more common in patent ductus and in *V.S.D.* with pulmonary plethora, as an expression of an increased mitral blood flow into a dilated left ventricle.

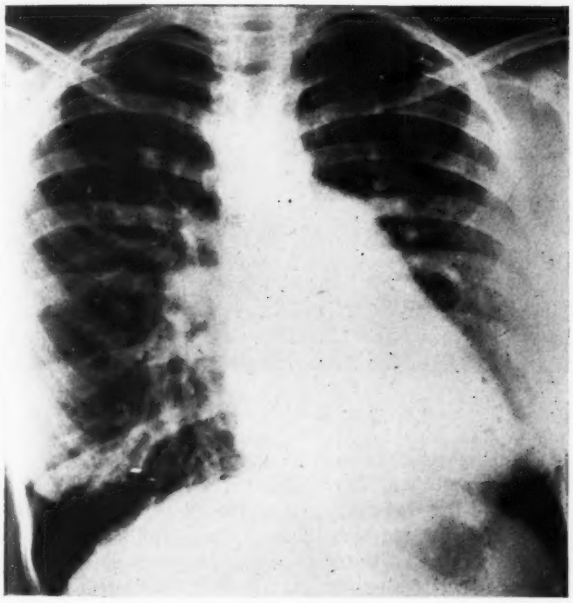

FIG. 10.—Skiagram showing dilatation of the pulmonary artery and pulmonary plethora in a case of ventricular septal defect. The left ventricle is enlarged, but this is not obvious in the view shown (i.e. it could be the right).

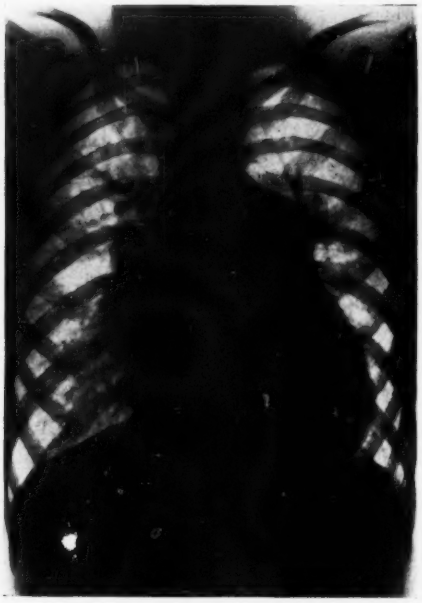

FIG. 11.—Skiagram showing dilatation of the pulmonary artery and pulmonary plethora in a case of patent ductus arteriosus. The left ventricle is enlarged.

The radiological appearances are of course very important, but they may not distinguish *A.S.D.* from *V.S.D.* (Fig. 10) or patent ductus (Fig. 11), and they are not always obvious in mild cases (Fig. 12 and 13). The chief value of fluoroscopy is to demonstrate pulmonary plethora and enlargement of the right ventricle, and it is true that *A.S.D.* can be distinguished in most cases in this way; but it is not always easy to be sure that enlargement is entirely right-sided, and skiagrams in the postero-anterior position may be particularly misleading in this respect, the appearances in *A.S.D.*, *V.S.D.*, and patent ductus being sometimes indistinguishable.

The electrocardiogram provides extremely helpful information, for the diagnosis of *A.S.D.* is almost untenable in the absence of partial or complete right *B.B.Bl.* Again, under the clinical circumstances, the presence of right *B.B.Bl.* at once makes *A.S.D.* the probable diagnosis, the chances being about ten to one in its favour. When partial right *B.B.Bl.* occurs in a case of *V.S.D.* or patent ductus, there is usually some evidence of left ventricular enlargement, particularly a deep Q wave and tall R wave in left ventricular surface leads, and a relatively deep S wave in lead V 1; occasionally, there is also depression of the S–T segment or even inversion of the T wave in leads V5 or 6. It is rare to meet obvious right *B.B.Bl.* in these conditions. The diagnostic importance of wide splitting of the second heart sound is due entirely to its indicating right *B.B.Bl.*

FIG. 12.—Skiagram in a relatively mild case of *A.S.D.* Diagnostic signs are present, but are not advanced.

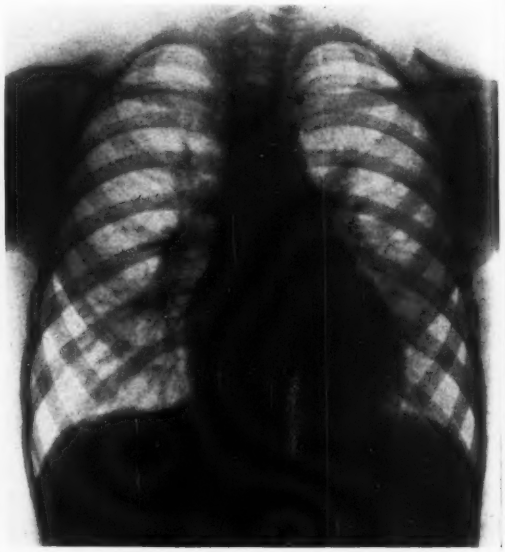

FIG. 13.—Skiagram from a relatively mild case of *A.S.D.*, showing minimal changes.

The data presented in no way determine whether right *B.B.Bl.* in atrial septal defect is caused by a local congenital or acquired lesion of the right bundle branch, or whether it results from dilatation of the right ventricle. There can be little doubt, however, that dilatation of a ventricle may produce the electrocardiographic pattern of homolateral bundle branch block both experimentally (Rasmussen, 1942) and clinically—in massive pulmonary embolism for instance. The discovery of delayed conduction in infancy or early childhood does not favour a congenital anomaly of the bundle in question, for dilatation of the right ventricle must occur as soon as the shunt operates.

The absence of prominent pulmonary P waves is interesting in view of the relatively low right ventricular pressures recorded in this series, and harmonizes with previous work suggesting that the tall spiked P wave is indirectly related to a high right ventricular pressure (Wood, 1948).

In differential diagnosis the following rules have been found valuable.

1. A normal heart with a pulmonary systolic murmur, relatively conspicuous pulmonary artery, and grade II splitting of the second heart sound may suggest *A.S.D.*, but may be distinguished by a normal electrocardiogram.

2. Idiopathic dilatation of the pulmonary artery with pulmonary incompetence may give rise to right *B.B.Bl.*, but may yet be recognized by the absence of radiological evidence of pulmonary plethora, dilatation being limited to the trunk or main branches of the pulmonary artery.

3. Simple pulmonary valvular stenosis with dilatation of the pulmonary artery presents no problem, because the second heart sound is single.

4. Patent ductus arteriosus without a machinery murmur and perhaps with pulmonary incompetence is easily distinguished by the water hammer quality of the pulse.

5. *V.S.D.* with pulmonary plethora and with a high or unimpressive basal systolic murmur and thrill and partial right *B.B.Bl.* may be very confusing, but may be recognized by electrocardiographic or radiological evidence (in the second oblique position) of left ventricular enlargement.

Cardiac catheterization offers convincing proof of *A.S.D.* except in rare late cases in which the shunt is reversed, and should be undertaken in all doubtful instances. The shunt is nearly always considerable, and averages about one and a half times the systemic blood flow, i.e. it is of the order of 6 to 7 litres a minute. The difference in the oxygen content between samples from the superior vena cava and samples from the right auricle, right ventricle, and pulmonary artery have always been well beyond the range of technical error or spontaneous variation. Another very constant finding has been the remarkable absence of pulmonary hypertension. That patients with *A.S.D.* may remain active and free from symptoms for so long emphasizes again the fact that the heart is less embarrassed by pumping an increased volume of blood than it is by pumping against increased resistance.

Summary and Conclusion

A series of 62 cases of atrial septal defect is presented.

A clinical diagnosis may be made in most instances if an acyanotic child or adult, with few if any symptoms, presents a small or normal peripheral pulse, tapping or tumultuous cardiac impulse, lifting right ventricular outflow tract, pulmonary systolic murmur with or without a thrill, pulmonary diastolic murmur, and wide splitting of the second heart sound.

Wide splitting of the second heart sound is attributed to right *B.B.Bl.* or to delay in the emptying time of an over-filled right ventricle, and is a far more important sign of *A.S.D.* than accentuation of the pulmonary second sound.

The electrocardiogram shows partial or complete right *B.B.Bl.* in 95 per cent of cases; indeed the diagnosis of *A.S.D.* is untenable in its absence, unless proof is obtained by means of cardiac catheterization.

A conspicuous P pulmonale is no part of the electrocardiographic pattern of *A.S.D.*

X-ray appearances may be diagnostic of *A.S.D.* if evidence of pulmonary plethora can be shown to be associated with enlargement of the right ventricle only; but this is not always possible. Skiagrams in cases of *V.S.D.* or patent ductus present similar evidence of pulmonary plethora and can only be distinguished if enlargement of the left ventricle can be recognized with certainty.

The radiological changes in mild cases of *A.S.D.* in children may be scarcely beyond the limits of normal variation.

Cardiac catheterization was performed in 21 of the 62 cases of *A.S.D.* presented. Samples from the right auricle, right ventricle, and pulmonary artery were usually between 80 and 90 per cent saturated; samples from the venæ cavæ were normal (about 70% saturated.) The difference was always well beyond the limits of technical error or spontaneous variation. The pulmonary blood flow averaged about two and a half times the systemic flow.

Absence of pulmonary hypertension was constant and noteworthy. Obvious accentuation of the pulmonary element of the second heart sound does not favour a diagnosis of atrial septal defect.

We wish to thank the consulting staff of the National Heart Hospital for allowing us to investigate and present some of their cases; particularly Sir John Parkinson who also helped us in other ways.

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ANGIOCARDIOGRAPHY IN HEART DISEASE IN CHILDREN

BY

RODOLFO O. KREUTZER, JUAN A. CAPRILE, AND FREDERIK M. WESSELS

From the Cardiac Clinic, Children's Hospital, Buenos Aires, Argentina

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We present here some of our experience of angiocardiography; it deals exclusively with children and infants as a result of our working in a children's hospital.*

When a careful clinical examination, electrocardiograms, X rays, and the simple laboratory tests do not make the diagnosis certain, we have two principal procedures: heart catheterization with study of the pressures and gas content from samples obtained in different chambers of the heart, and in addition, angiocardiography. Although the first procedure is of great value, it is very difficult to perform on young children because of their small veins and lack of co-operation. On the contrary, angiocardiography is simple and harmless as far as our experience shows.

Although the extensive and careful study Taussig made of the clinical and radiological picture of the different congenital heart malformations means a very great aid to diagnosis, we still believe that, especially in infants, angiocardiography can be a great help. At this early age diagnosis is difficult because the heart has not acquired its typical form and the physical and electrocardiographic signs are not yet clearly evident. It is also at this stage that the angiocardiograms are clearest as is illustrated by some of the pictures shown here. Therefore, we consider angiocardiography essential in diagnosing congenital heart diseases in infants, and certainly of great help even if not essential in older children.

Historical

The first attempt was made by Forssmann in 1929; after introducing a rubber catheter as far as the right auricle, by way of a vein in his own arm, he made a trial at visualization by injecting some opaque material and taking X rays.

After this, Moniz, Carvalho, and Lima in 1932; Conte and Costa in 1933; Ravina, Sourire, and Benzaquen in 1932; and Ameuille *et al.* in 1936 made several attempts to visualize the right cavities of the heart and mainly the pulmonary arteries in animals and men, all more or less following Forssmann's technique. In 1933, Reboult and Racine visualized very distinctly in dogs the right and left cavities of the heart, the aorta, and the coronary arteries, by introducing a needle directly into the heart and injecting a radio-opaque substance.

In 1937, Castellanos, Pereiras, and Garcia from Havana, Cuba, obtained for the first time a good visualization of the right side of the heart, pulmonary artery, and its branches in living children, after injecting perabrodil 35 per cent directly into a vein of the arm. They were the first to use the term " angiocardiography " which has become classical, and they pointed out the simplicity of the method and its value in the diagnosis of congenital heart disease.

Shortly afterwards, Robb and Steinberg, 1938 and 1939, in New York, used for the first time 70 per cent diodrast and a mechanical cassette changer, thus obtaining good visualization of the left side and aorta as well as the right. They used this procedure successfully on adults, which Castellanos, Pereiras, and Garcia had been unable to do, because of the lack of an adequate contrast

* When one of the authors (R. K.) was in England recently, the editor was interested seeing his clear and striking angiocardiograms and suggested that he might submit a paper on the subject for publication in the B.H.J. (M. C.).

medium. They emphasized the value of this method in studying the topography of the heart and in the differential diagnosis of mediastinal tumours and various cardiac diseases.

Stewart, Breimer, and Maier were the first to take a motion picture of the fluoroscopic image, and others took photographs of it, the results not being as clear as ordinary X rays. Chavez *et al.*, going back to Moniz's method, injected the opaque substance through a catheter, introduced into the jugular vein up to the right auricle, and obtained very clear pictures.

Further work has been done on the subject by many others including Sussman and Grishman, Taylor and MacGovern, Keele, Thoyer-Rozat and Piquet, and Carson and his associates. Dotter and Steinberg (1949) have published their experiences with more than a thousand angiocardiograms taken during the last eleven years.

In our country, Spangenberg *et al.* (1942) and Kreutzer, Pelliza, and Calisti (1944) made the first publications in this field. Segura *et al.*, Pennington, and Malenchini have also worked in this line.

Technique

No special preparation of the patient is necessary except that he must have had nothing to eat during the previous four hours. As the intracutaneous and intra-ocular sensitization tests are not very accurate, we do not use them. However, in patients with an allergic history, we inject intravenously 2 ml. of the iodine compound used and, if there is no reaction five minutes later, we inject the rest.

We have used several different compounds (iodoxil, nosylam, perabrodil, neo-iopax), but the best results were obtained with diodone (official British pharmaceutical name), 75 per cent solution with 51·5 per cent iodine which is sold in our country under the name nitasom and in England as pyelectan. The manufacturers warn against the use of this contrast medium in angiocardiography, saying that it is painful and that when it is injected outside the vein it produces abscesses, but in our experience we have not had such a consequence. The amount to be used varies with the age: 10 ml. in the newborn, 12 ml. up to 3 months, 15 ml. up to 1 year, and from then on we calculate about 1·5 ml. per kilo body weight; an average of 20 ml. for children up to 3 years, 30 ml. up to 6, and about 60 ml. for adults. We consider that less than 1 ml. per kilo body weight is insufficient, especially when there is cardiac enlargement.

The syringes we use do not differ from the ordinary except that the hole in the cone must be large. The diameter of the needle used varies with the age of the patient: 10/10 mm. in the new born 12/10 mm. in the infant, 15/10 mm. in children up to 3 years, it being necessary to use at least 20/10 mm. when the injection is of 30 ml., and 30/10 mm. if it is more. The injection is made directly through the skin without exposing the vein,* with local novocaine anæsthesia. We never use a general anæsthetic. Very seldom, even in small infants, have we found it impossible to introduce the needle into a vein, and for this reason we believe the dissection of the vein unnecessary. The injection should be made very rapidly, in less than 1·5 seconds.

The films are taken at a distance of 1 meter with 100 ma. in 1/10 sec., the kilovoltage varying according to the thickness of the thorax, but using about 25 per cent more than the usual for the exposure of the heart.†

All the angiocardiograms are taken in the horizontal position on a cassette changer described by one of us (R.K.) in a previous paper, and in the left anterior oblique position (because we consider this the one in which the four cavities of the heart are best seen), unless the previous clinical examination suggests that another would be better. Four films are taken with one second between them, unless we are especially interested in the left side of the heart, and then the last two are somewhat delayed.

Immediately after the injection, a sensation of heat is usually felt as well as palpitation, itching, and frequently a severe headache; vomiting may occur shortly afterwards. Generally, a great thirst follows and even infants take water avidly. All these reactions last only a few minutes. In

* The injection is made by Dr. Juan Marletta.
† The roentgen technique is under the supervision of Dr. Sofio Calisti.

taking more than 400 angiocardiograms we have lost only one patient, an infant with complete transposition of the great vessels, who died 12 hours after the procedure, with high fever (41° C.) and convulsions.

Presentation of Material

We have purposely selected those cases that were substantiated by necropsy or operation. We need not give a detailed description of the normal angiocardiogram as this has already been done by others. We show only two views taken in the left anterior oblique position, because this is the one we ordinarily use.

A normal dextro-angiocardiogram is shown in Fig. 1. The dye is seen in the right humeral and subclavian veins (1); the superior vena cava is already empty; the right cavities are well filled; it is difficult to differentiate the right auricle (2) from the ventricle (3) as they lie on the same level, one directly back of the other; the interventricular septum is straight and is parallel to the spinal column; the main pulmonary artery (4), and the left pulmonary artery (5) are clearly seen, whereas, from the right pulmonary artery (6) only the finer branches are seen.

A normal lævo-angiocardiogram is seen in Fig. 2. After passing through the lungs, the dye fills the left cavities (1); the aorta is well filled (2) and from its arch emerge the following vessels; inominate artery (3) and its two branches, right carotid (4) and right subclavian (5); left carotid (6), and left subclavian (7) from which the vertebral is seen to arise; the descending aorta (8) can be

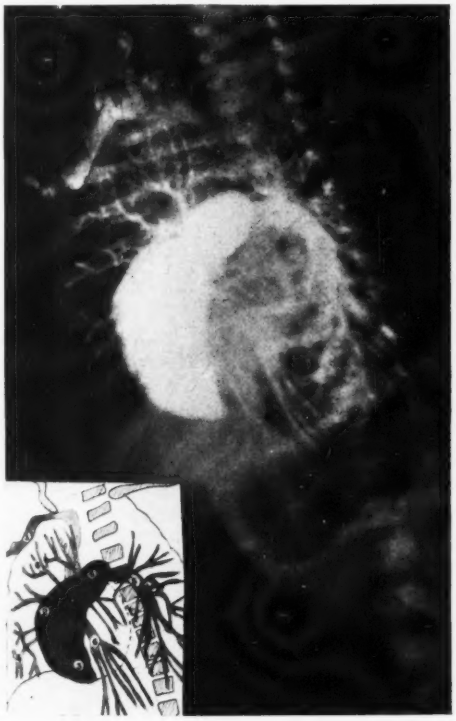

Fig. 1.—Normal dextro-angiocardiogram in left antero-posterior position from infant, aged 5 days. For explanation and figures see text.

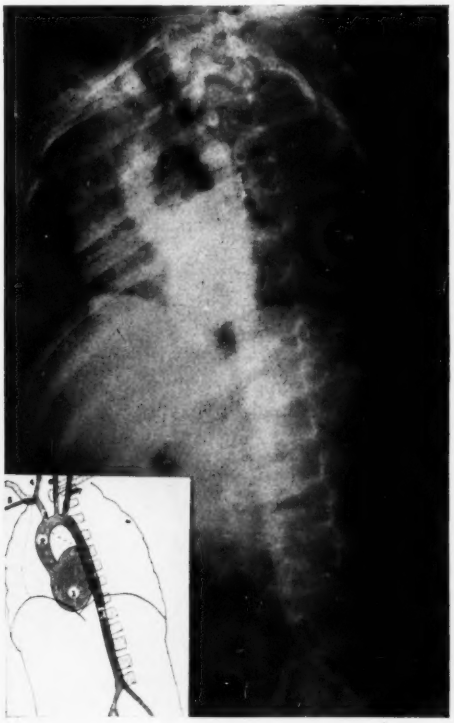

Fig. 2.—Normal lævo-angiocardiogram in left antero-posterior position from a child, aged 3 years (see text).

clearly distinguished up to its division into left and right iliacs; the aorta is curved in the form of a cane handle sharply bent; the interventricular septum is straight and parallel to the spinal column. In the left anterior oblique position, the anterior border of the ascending aorta does not form, at least in the child, the anterior part of the vascular shadow at the base of the heart. Under the aortic arch is seen the normal clarity of the vascular window.

Atelectasis of the Right Lung

M.T.C., aged 26 days. Normal until 15 days when fever, dyspnœa, and cyanosis appeared. The child was found to be poorly developed, acutely ill, cyanotic, and gasping for breath; the heart was percussed on the right; the cardiac sounds were faint and no murmurs were heard. Based on the X-ray a diagnosis of dextrocardia and congenital heart disease and bronchial pneumonia was made by the doctor who sent the child to us. Although we suspected atelectasis of the right lung to be the main cause of his distress, basing our belief on the normal electrocardiogram and the displacement of the mediastinum to the right, we made an angiocardiogram which is shown in Fig. 3.

The typical U-shaped contour described by Castellanos *et al.* (1937) is seen. Superior vena cava (1); right auricle (2); right ventricle (3); main pulmonary artery (4); the right pulmonary artery has a horizontal position closing the upper part of the U (5); the left pulmonary artery (6) helps together with the main pulmonary artery to form the middle segment of the left border of the heart. The interventricular septum is straight and parallel to the spinal column, thus following a different direction from the interventricular groove. In looking at this angiocardiogram we were surprised to find that the heart was in its normal position, which fact was further substantiated by a second X-ray. The patient had had a severe coughing attack while being made ready for the angiocardiogram, which probably helped to clear the bronchi and expand the lungs.

Agenesis of the Right Lung

M.S., aged 1 month. Dyspnœa and slight cyanosis from birth; large umbilical hernia operated on a few days before. A poorly developed, cyanotic child, breathing rapidly. The apex was thought to be palpated on the right. Electrocardiogram: right axis deviation but not a mirror image in the first lead as would be expected in a dextrocardia. X ray: the heart on the right side of the chest, the left lung introducing itself into the right hemithorax. After barium, the stomach could be seen on the left; the liver is seen on the right side and is considerably enlarged.

The angiocardiogram (Fig. 4) taken at the same time shows the humeral vein (1); subclavian, superior vena cava, right cavities (2) from which a good sized pulmonary artery emerges, continuing into a voluminous left pulmonary artery. The left ventricle is also filled (3), and the aorta (6) whose arch makes a loop can be seen up to its division into two iliacs. The circulation in the left lung is clearly seen, but on the right no pulmonary artery and no circulation is visible. Therefore, agenesis of the right lung was suspected. An interventricular septal defect, through which the left ventricle and the aorta had filled, was also diagnosed.

The patient died due to the rupture of the umbilical hernia and the autopsy confirmed the clinical diagnosis: agenesis of the right lung, the trachea continuing directly into the left bronchus; interventricular septal defect with the aorta emerging completely from the left ventricle; a big pulmonary artery coming off the right ventricle gave only one branch, the left one, which was even larger than the aorta.

Tetralogy of Fallot and Persistent Ductus Arteriosus

M.C.P., aged 8 days. Persistent cyanosis from birth with frequent attacks of increased cyanosis and dyspnœa, in some of which he lost consciousness. The heart sounds were normal, no murmurs. Electrocardiogram, right axis deviation. Fluoroscopic examination shows an enlarged heart and clear lung fields. As is usual at this age, the form of the heart did not contribute to the diagnosis of the malformation.

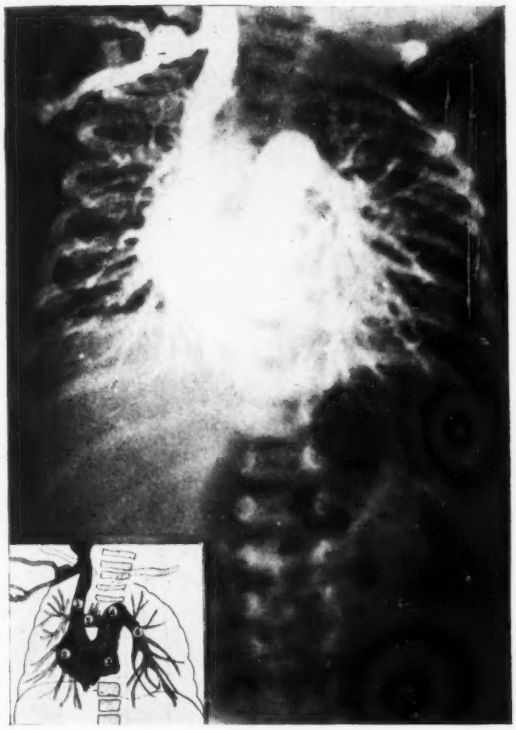

FIG. 3.—Dextro-angiocardiogram from infant with atelectasis of the right lung (see text).

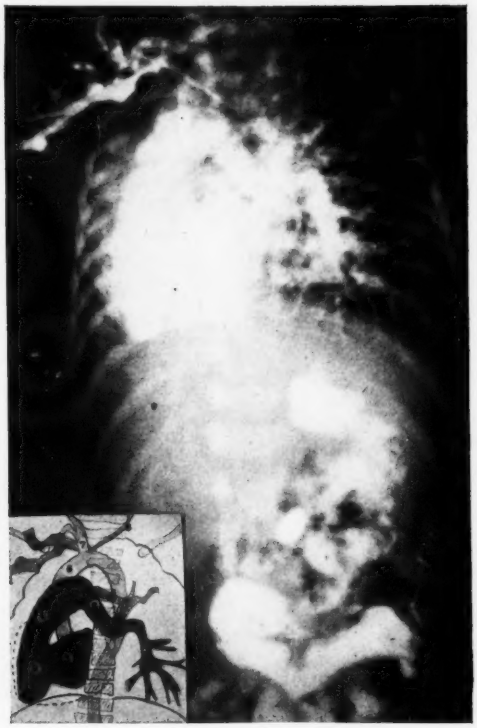

FIG. 4.—Dextro-angiocardiogram from an infant of one month with agenesis of the right lung (see text).

The angiocardiogram (Fig. 5) shows superior vena cava (1); right auricle (2); right ventricle (3); and the simultaneous filling of the aorta (10) and pulmonary artery. The latter emerges from the right ventricle through a very narrow pulmonary conus (4). The small size of the pulmonary valves (5) and both pulmonary arteries is noticeable. Number (6) shows the section of the right pulmonary artery and (13) shows the left. A strip connecting the lower border of the aortic arch (12) with the left pulmonary artery was considered to be the persistent ductus (11).

Based on these findings, we made a diagnosis of tetralogy of Fallot with extreme pulmonary stenosis and persistent ductus arteriosus, and to the closure of the latter we attributed the death of the patient a few weeks later.

Tetralogy of Fallot with Anomalous Distribution of the Vessels from the Aortic Arch

O.C.D., aged 4 years. Dyspnœa from birth; increasing cyanosis from the age of one year. Repeated attacks of dyspnœa and cyanosis with loss of consciousness. Not yet able to walk. Clubbing of the fingers and toes; loud, harsh systolic murmur, maximal in the second intercostal space to the left of the sternum. Electrocardiogram, marked right axis deviation. On fluoro-, scopy, the heart was seen to be somewhat enlarged; no prominence of the pulmonary conus; the aortic knob was on the left; the lung fields and pulmonary window were unusually clear. The diagnosis of tetralogy of Fallot was made.

The angiocardiogram confirmed the diagnosis and showed also the anomalous distribution of

the vessels from the aortic arch. Fig. 6 shows superior vena cava (1); right cavities normally filled (2); some of the dye entering the left ventricle (6) through the interventricular septal defect. The simultaneous filling of a large aorta (4) and a very small pulmonary artery (3) is seen. Four branches come off the aorta: first the very big right carotid (7), the much smaller left carotid (8), the left sub-clavian artery (9), from which the vertebral emerges, and finally the right subclavian artery which originates in the posterior surface of the aortic arch (5), emerging as the last branch from it. The right subclavian runs between the trachea and the œsophagus, and its pressure on the trachea probably contributed to his respiratory difficulty. The patient died and the necropsy confirmed these observations.

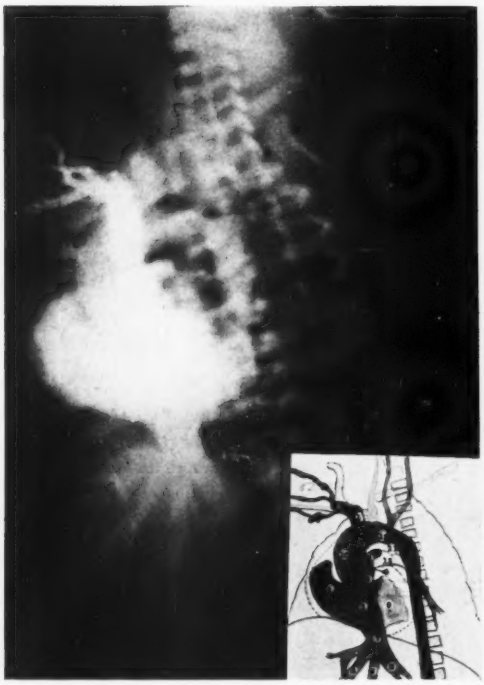

FIG. 5.—Dextro-angiocardiogram from a case of tetralogy of Fallot and persistent ductus arteriosus (see text).

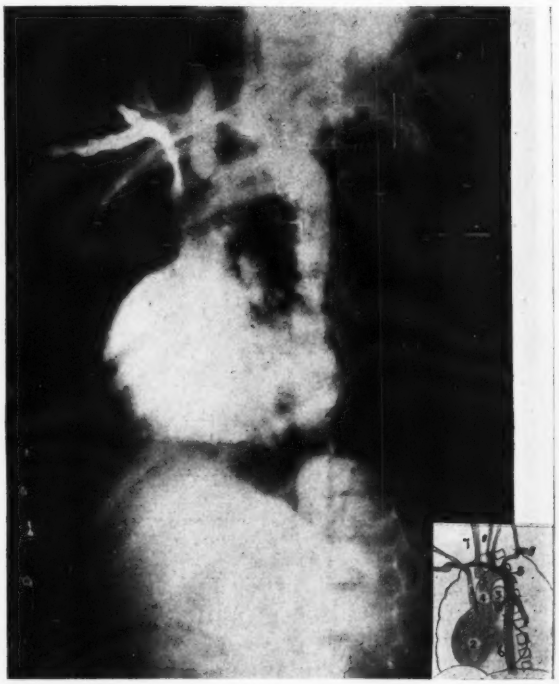

FIG. 6.—Dextro-angiocardiogram from a case of tetralogy of Fallot with anomalous distribution of the vessels from the aortic arch (see text).

Persistent Ductus Arteriosus

As angiocardiography is not the ideal procedure for the diagnosis of isolated persistent ductus arteriosus, Castellanos and Pereiras originated a method of direct visualization of the aorta, whereby the dye passes into the pulmonary artery through the ductus.

The direct angiocardiographic signs of persistent ductus arteriosus are: (*a*) *the visualization of the ductus itself*, very rarely seen in cases of isolated ductus, bu' more frequently seen when there are other malformations (Fig. 5 and 10), and (*b*) *visualization of the infundibulum of the ductus*—the aortic end of the ductus has an infundibular form which can be seen on the lævo-angiocardiogram. This was proved by Sussman and Grishman by attaching metal clips alongside the ductus during operation, and they described it as a " localized dilatation of the aorta on its anterior aspect just

beyond the isthmus." In presenting a case, Keele (1948) showed that this convexity persisted after the ligation of the ductus, but that the prolonged or renewed filling of the pulmonary artery was no longer seen.

Their are three indirect signs. (*a*) *Visualization of the aorta in the first films*, as has been seen by Landivar and Martiarena (1947). The occurrence of this sign is very unusual unless there is also coarctation of the aorta in the infantile type, when the descending aorta is almost continuous with the ductus. (*b*) *Renewed filling of the pulmonary artery* in the lævo-angiocardiogram. This has more value when it is combined with the visualization of the infundibulum. (*c*) *Dilatation of the main pulmonary artery and its left branch as well as its elevation*, probably produced by the pulling of the ductus toward the aorta. This sign is found in many other instances in which the pulmonary artery is also large, such as auricular septal defect and congenital dilatation of the pulmonary artery with valvular stenosis.

J.L., aged 7 years. Heart murmur discovered during routine examination. The apex palpated in the fifth left intercostal space in the mid-clavicular line. Systolic thrill and murmur loudest at the second left intercostal space to the left of the sternum. Blood pressure 85/0. Fluoroscopic examination: heart slightly enlarged, prominent pulmonary conus with vigorous pulsation; increased pulmonary shadows and hilar dance. It seemed likely that this patient had a patent ductus, but the absence of a continuous murmur and the right axis deviation impelled us to take an angiocardiogram to make sure there was no pulmonary stenosis.

The dextro-angiocardiogram (Fig. 7) shows the superior vena cava (1); the right cavities (2–3) normally filled; and (4) the dilatation and elevation of the main pulmonary artery. This angiocardiogram excluded pulmonary stenosis and showed an indirect sign of patent ductus; these two facts caused us to advise the operation, which confirmed the diagnosis.

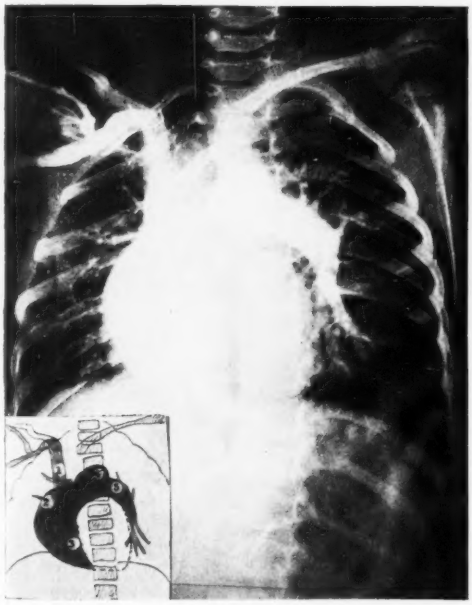

FIG. 7.—Dextro-angiocardiogram from a case of patent ductus arteriosus (see text).

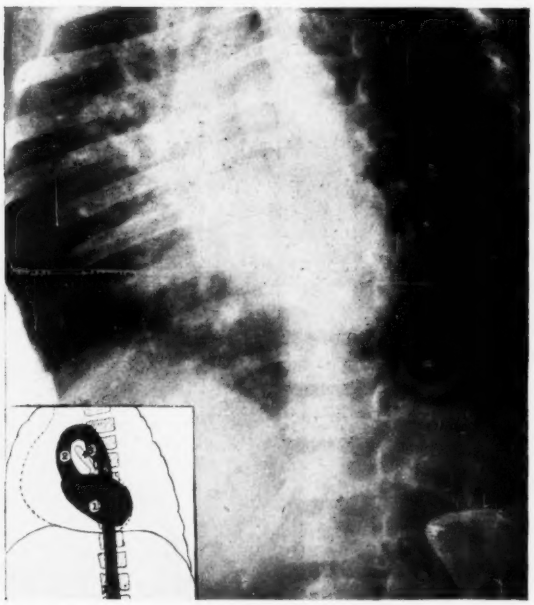

FIG. 8.—Lævo-angiocardiogram from a case of patent ductus arteriosus (see text).

F.S., aged 3 years. Never had any symptoms: a continuous machinery murmur discovered accidentally. Electrocardiogram normal. Fluoroscopy showed heart somewhat enlarged, prominent pulmonary conus, and bilateral hilar dance.

The lævo-angiocardiogram (Fig. 8) shows the left cavities filled (1); the aorta (2); the prominence on the anterior aspect of the descending portion of the aortic arch (3), which corresponds to the infundibulum of the ductus; the refilling of the pulmonary artery (4)—which occupies the vascular window—is also seen, when the right ventricle has already emptied.

This patient was operated on and the murmur disappeared completely. A year later, a ten-months-old brother of this child was diagnosed as having a patent ductus with cardiac insufficiency and was also operated on successfully.

Infundibular Stenosis with Dilated Pulmonary Artery

In these cases the dextro-angiocardiogram shows a characteristic picture which we have called " racket sign "; the stenosed portion corresponds to the handle, and the dilated pulmonary artery to the racket itself. Similar pictures have been shown by different authors (Keele, Dotter, Steinberg). This sign is clearly shown in the following case of a patient upon whom we considered operating before the angiocardiogram was taken. Therefore, even though the angiocardiogram may not be very valuable in the diagnosis of the patent ductus, we consider that it should be taken before recommending operation, whenever the clinical signs are not convincing or pronounced right axis deviation arouses the suspicion of pulmonary stenosis.

M.E.A., aged 8 years. Murmur accidentally discovered when the patient was three years of age; systolic thrill and harsh, loud systolic murmur over the second interspace to the left of the sternum. Blood pressure 100/70. Electrocardiogram, tendency to right axis deviation. X ray: no enlargement of heart, great prominence of the pulmonary conus with pulsation, and bilateral hilar dance.

The dextro-angiocardiogram (Fig. 9) shows a nice example of " racket sign." The dye is seen in the superior vena cava (1); the right auricle (2); the right ventricle (3); the stenosed infundibulum (4); and the dilated pulmonary artery (5), the two latter forming the racket. Also the dilated left (6) and right (7) branches of the pulmonary artery are seen. This same racket sign was seen on the angiocardiogram taken in the oblique position. We think that this child has pulmonary stenosis, proved by both angiocardiograms, and we presume she has also a patent ductus which would explain the hilar dance.

Complete Transposition of the Great Vessels

Although the clinical and radiological picture of this malformation has been beautifully described by Taussig, the angiocardiogram can be of great aid in the diagnosis. Although the only patient we have lost (whose death could be attributed to the angiocardiography) had a complete transposition of the great vessels, we do not believe the procedure to be especially dangerous in this malformation. In these cases, the dextro-angiocardiogram in the left anterior oblique position shows the early filling of the aorta which rises anteriorly from the right ventricle and whose arch has the form of a cane handle only slightly bent. The pulmonary artery is evident in the later films.

G.E., aged 5 days. Cyanosis and dyspnœa from birth with attacks of loss of consciousness, so frequent and lasting so long that they seriously endangered his life. Heart sounds normal; no murmurs. The X-ray showed the heart somewhat enlarged, absence of pulmonary conus, the vascular shadow at the base of the heart narrower in the anterior posterior than in the oblique position. Electrocardiogram, marked right axis deviation.

The dextro-angiocardiogram (Fig. 10) shows superior vena cava (1); right auricle (2); right ventricle (3); and a small amount of dye in the left auricle (9). From the right ventricle, the aorta

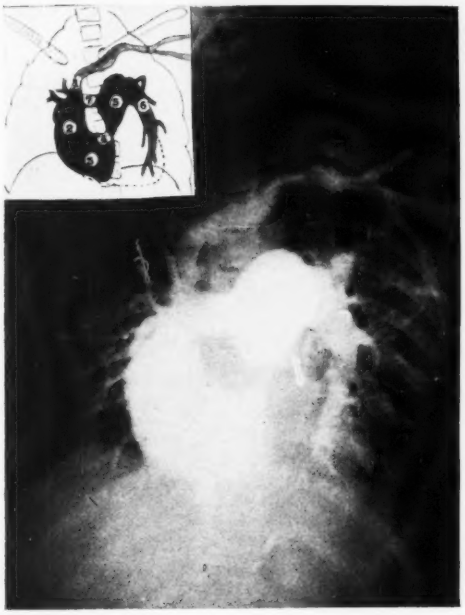

FIG. 9.—Dextro-angiocardiogram from a case of infundibular pulmonary stenosis with dilated pulmonary artery (see text).

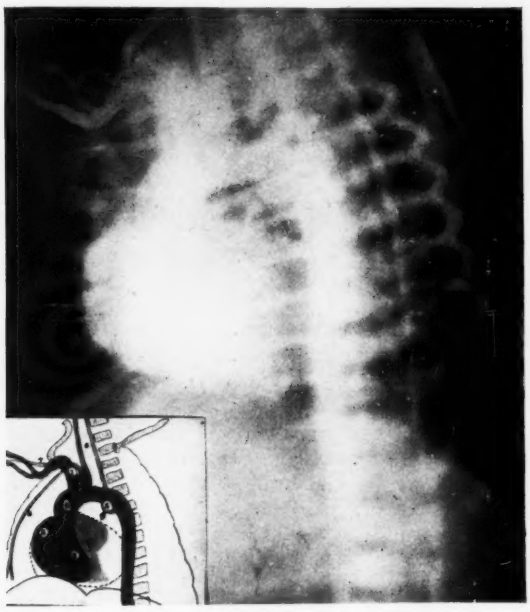

FIG. 10.—Dextro-angiocardiogram from a case of complete transposition of the great vessels (see text).

is seen to arise, its arch forming an open curve. The bulge (5) was thought to be the infundibulum of a patent ductus arteriosus and the little strip arising from it to be the ductus itself. From the aortic arch the main vessels arise and several of its branches are seen. In the later films the left branch of the pulmonary artery is seen.

At the time we saw the patient, and based on the angiocardiogram, we incorrectly diagnosed the case as a tetralogy of Fallot. Now, having a better knowledge of the angiocardiographic picture of transposition of the great vessels, it seems unlikely that we would make the same mistake again. The necropsy revealed a complete transposition of the great vessels with an auricular septal defect and a patent ductus arteriosus.

Coarctation of the Aorta

Although the direct visualization of the aorta by means of the injection of the dye through a catheter introduced through a humeral or carotid artery is a better method for the study of this malformation, the angiocardiogram may be helpful in determining the site of the coarctation as well as to show the pathways of the collateral circulation.

J.C.R.*, aged 5 years. From the age of 4, complained of pains in both legs. At the age of 6 found to have a murmur and treated as rheumatic fever. On examination, he was found to have a rough, loud systolic murmur over the entire præcordium and a short, low-pitched diastolic murmur at the apex. No femoral pulse was palpable. Blood pressure, 180/130 in the arms. Electrocardiogram, tendency to *right* axis deviation.

* This case was reported before the *Sociedad Argentina de Cardiologia.*

The lævo-angiocardiogram (Fig. 11) shows the left cavities filled (1); and the aorta (2) arising from the left ventricle with its branches. After the emergence of the left subclavian, the shadow cast by the aortic arch is suddenly interrupted as is shown by the arrow (6). The patient was operated on, and a complete occlusion of the aorta was found 1 cm. under the place where the left subclavian arose.

Taussig's Syndrome

Taussig and Bing (1949) described the clinical picture of the complete transposition of the aorta and the over-riding of the pulmonary artery. The case presented here was diagnosed as such a malformation, the diagnosis being sustained by the angiocardiogram.

A. del V., aged 8 years. Cyanosis from early in life; squatting when tired; harsh, loud systolic murmur over entire præcordium. X-rays showed heart not enlarged, a prominent pulmonary conus, and a bilateral hilar dance.

The dextro-angiocardiogram (Fig. 12) shows the normal filling of the right cavities (2–3) through the superior vena cava (1); the aorta (5) arises entirely from the right ventricle and its arch forms an open curve, as is usually seen when this vessel is transposed. The pulmonary artery (4) of normal size is seen to arise behind the aorta and probably over-rides the septum. A small amount of dye has entered the left ventricle through the ventricular septal defect.

FIG. 11.—Lævo-angiocardiogram from a case of coarctation of the aorta (see text).

FIG. 12.—Dextro-angiocardiogram from a case of Taussig's syndrome (see text).

Mediastinal Tumour (Hydatic Cyst)

T.B., aged 9 years. Admitted to hospital with diphtheria. On examination, slight generalized cyanosis and moderate clubbing of the fingers; a harsh, loud systolic murmur at the left base. Electrocardiogram, right axis deviation. X ray (Fig. 13) showed heart of normal size and a great prominence in the region of the pulmonary conus, which, on fluoroscopy was seen to pulsate vigorously. The possibility of an hydatic cyst was considered, but the Ghedini reaction was negative and the Casoni reaction only very slightly positive.

FIG. 13.—Teleradiogram from a case of mediastinal tumour (hydatic cyst).

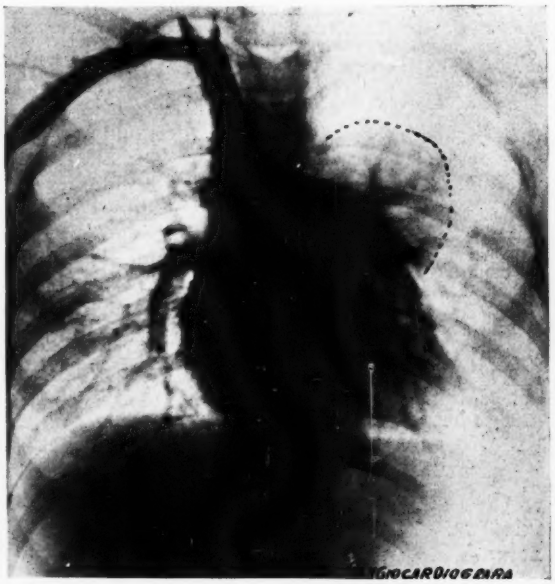

FIG. 14.—Dextro-angiocardiogram from the same case of mediastinal tumour.

Considering the possibility of a congenital malformation of the heart, an angiocardiogram (Fig. 14) was taken, showing the complete independence of the tumor from the pulmonary artery. In consequence, the pulsations we saw on fluoroscopy were transmitted from the pulmonary artery. The patient was operated on, with the diagnosis of congenital cyst. Much to our surprise an hydatic cyst was discovered and was successfully removed. After the operation, the cyanosis, the clubbing, and even the murmur disappeared completely. This suggests that she really had a pulmonary stenosis produced by the compression of the cyst on the pulmonary artery.

SUMMARY AND CONCLUSIONS

We practice angiocardiography using iodoxil as the contrast medium, without exposing the vein and without general anæsthesia.

Here we present a series of angiocardiograms to demonstrate its value in:

(*a*) the study of the radiological topography of the cardiovascular silhouette,
(*b*) the diagnosis of pulmonary atelectasis and pulmonary agenesis,
(*c*) the diagnosis of the different congenital malformations of the heart, and
(*d*) the differential diagnosis of mediastinal tumours.

We consider angiocardiography the procedure that gives the most valuable information in the diagnosis of congenital heart disease during infancy.

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PRIMARY PULMONARY HYPERTENSION

BY

W. D. BRINTON

From Guy's Hospital

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Primary pulmonary vascular sclerosis was first fully described by Brenner (1935) who stressed the presence of hypertrophy of the right, but not of the left ventricle; he concluded his description with the opinion that primary sclerosis is not a pathological entity but includes several conditions. Other authors, notably De Navasquez *et al.* (1940), preferred the term " primary or idiopathic right ventricular hypertrophy." Until recently pulmonary hypertension was an assumption from the physical signs and morbid anatomy, but in the last few years evidence has accrued from cardiac catheterization that it does in fact exist in these cases.

By definition, in *primary* pulmonary hypertension, none of the known causes of pulmonary hypertension are present: it is therefore not surprising that few suggestions as to the cause are reported. The only experimental evidence available is that of Harrison (1948) who, working on rabbits, produced lesions in the smaller pulmonary arteries morphologically indistinguishable from spontaneous arteriosclerosis, by means of intravenous injections of finely fragmented fibrin. He was unable to produce significant hypertrophy of the right ventricle.

The purpose of this paper is to record a possible cause for some of these cases.

Case Notes

S.B., aged 26, was admitted to Guy's Hospital under Dr. Mann on February 23, 1949, complaining of shortness of breath for 18 months and loss of voice for one week.

He had a normal childhood and worked as a labourer until he joined the army in 1939. In 1945, in India, he had dysentery; he was in hospital for 6 weeks and was given tablets, but no injections, and made a good recovery. In 1946, in Burma, he was admitted to hospital complaining of right-sided pain, first thought to be due to amœbic hepatitis but later considered to be due to pleurisy, probably of tuberculous origin. There was fever for 10 days without leucocytosis and the pain spread to the left chest. On one occasion fine crepitations were heard at both lung-bases and a chest X-ray showed " tenting " of the right diaphragm with small areas of infiltration at both bases. At no time was a rub heard and there was no effusion. Four days after the first X-ray, a second film showed that the infiltration had gone; and by now he was apyrexial and feeling well. However, he was sent home by hospital ship as a case of probable tuberculous pleurisy. On his arrival in this country he was noted to be perfectly well and to have no complaints; no physical signs of disease were found. The diagnosis of tuberculosis was abandoned therefore, and he was regraded in medical category C2, but kept in the army. In his army notes there is no mention of dyspnœa, of anæmia, or of any cardiovascular abnormality, but when later the patient observed the interest taken in his cardiac signs by those attending him at Guy's he stated that the army doctors had shown the same concern.

He was demobilized early in 1947 and worked as a labourer until October of that year when he began to notice shortness of breath. He went to the Royal Berkshire Infirmary, Reading, and was admitted. He was found to be pale (Hb. 70%) and his heart was enlarged. His blood pressure was 120/60. There were no signs of disease in the chest. Occult blood was found in the stools but

a barium meal showed no abnormality of œsophagus, stomach, or duodenum. An X-ray report at that time stated: " Heart mitral in shape with prominent hilar vascular shadows; the bases are clear."

He discharged himself after three weeks in hospital, but since that time his breathlessness on exertion had become progressively worse, so that for the last five months he had been unable to walk more than 100 yards without becoming acutely short of breath. There had been no pleuritic pain since 1947 and no cough, but he had recently experienced a dull retrosternal pain when short of breath.

A week before admission he developed a cold in the nose and sore throat with fever and a slightly productive cough. Later that day he suddenly lost his voice and complained of retrosternal dysphagia. The fever and cough had continued since, with mild pleuritic pain on the right side.

On admission he stated that for the last 18 months he had had severe hæmorrhage from piles, losing up to half a cupful of blood daily. His weight had been 13 stone in 1947 (in the army it was noted that he was somewhat obese); and it was now 10½ stone. He did not smoke or drink heavily.

On examination he was very pale and dyspnœic at rest. There was no cyanosis, no clubbing of fingers, and no glandular enlargement. His temperature was 99·0° F. The pulse was 120, regular with a few extrasystoles. The blood pressure was 110/60. The apex-beat was forceful and diffuse but was not outside the mid-clavicular line. There was a marked systolic heaving pulsation in the second and third left intercostal spaces alongside the sternum and there was a palpable second sound here. This region was dull to percussion. On auscultation there was a harsh systolic murmur at the apex and an even louder systolic murmur over the heaving pulsation at the base, where the second sound was extremely loud. There was a mid-diastolic added sound, audible all over the heart but loudest at a point just medial to the apex. There was no diastolic murmur. There was no filling of the veins of the neck and no œdema of the ankles. Laryngoscopy showed complete paralysis of the left vocal cord. In the chest, there was diminished air-entry and fine crepitations in the right axillary region. The liver was tender and enlarged to two fingers' breadth below the costal margin. There was no ascites. Rectal examination caused severe pain and spasm; no abnormality was felt, however, and there was no blood on the finger-stall.

The urine was normal throughout his illness. His hæmoglobin was 46 per cent with red cells 3·3 million. The white cells remained normal throughout. The chest X-ray showed slight cardiac enlargement (cardiothoracic ratio, 16/30 cm.), and dilatation of the pulmonary artery and its main branches (Fig. 1). There was no abnormality in the lung-fields. The electrocardiogram showed marked right axis deviation with flat T II and deeply inverted T III, due to right ventricular strain (Fig. 2). The Wassermann and Kahn reactions were negative.

Clinical course. He was transfused with a pint of fresh blood, but during the next few days he continued to run an intermittent fever up to 101° F. Blood cultures were sterile throughout his illness and examination of the sputum showed no abnormality. On the fourth day of admission he was started on penicillin. On the seventh day he had a sudden rigor, with temperature rising to 103° F. and pleuritic pain in the right chest. He became acutely ill with cyanosis of lips and fingertips and respirations at 40 a minute. He was placed in an oxygen tent and rallied somewhat. The next day he had another severe attack of air-hunger, this time with filling of the neck veins, and lumbar œdema was noted. Meanwhile the signs in his chest were unchanged. A further transfusion increased the signs of congestion. From then till his death on the tenth day after admission his temperature was subnormal. His general condition deteriorated, his air-hunger became continuous and was no longer relieved by oxygen. During the last four days he complained of severe pain beneath the sternum. He died in great distress, fighting for breath.

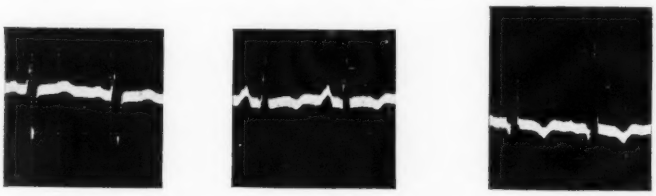
Clinical comment. On admission the signs of increased pressure and blood flow in the pulmonary artery suggested a diagnosis of auricular septal defect. The anæmia was considered to be due to chronic hæmorrhage from piles. There was no clinical evidence of mitral stenosis but he was always too ill to screen. Later, when the fever demanded attention, the possibility of a

subacute bacterial endocarditis had to be considered. The pleuritic pain was thought to be due to infarction, either from local thrombosis or by emboli if there were vegetations upon the defect. He had indeed a previous history of some inflammatory disease of the chest, but this seemed altogether too trivial to account for his symptoms by obliteration of the pulmonary vascular bed. Further, there was no clinical evidence of emphysema.

The great dilatation of the main pulmonary artery, which was the outstanding physical sign in this case, was taken to be the cause of the left cord paralysis by tension-traction on the recurrent laryngeal nerve. I have not been able to find a report of this complication in any previous case of primary pulmonary hypertension, but it has been described in cases of auricular septal defect by Erlanger and Levine (1943). In an interesting paper in which they add two further cases, one of mitral stenosis and the other a probable auricular septal defect, Dolowitz and Lewis (1948) support the hypothesis of Kraus (1901), that the process begins with enlargement of a strategically placed lymph-node with fixation of the left recurrent laryngeal nerve. After this fixation, enlargement of the aorta, of the pulmonary artery, or of the left auricle, could stretch and thus paralyse the nerve.

FIG. 1.—Teleradiograms of the chest, showing slight enlargement of the heart (cardiothoracic ratio 16 : 30) with prominent pulmonary conus and dilatation of main branches of the pulmonary artery.

During the course of this patient's illness, a pulmonary diastolic murmur was daily expected and carefully listened for. The dilatation of the pulmonary artery was fully sufficient to cause incompetence of the valve, but the murmur of regurgitation was never heard.



I. II. III.

FIG. 2.—Electrocardiogram, showing right axis deviation with flat TII and inverted TIII indicating right ventricular strain. V leads were not taken.

POST-MORTEM FINDINGS

The necropsy was performed by Dr. S. J. De Navasquez, about 10 hours after death. Only the relevant findings are given.

Cardiovascular system. The heart weighed 480 g., and of this the right ventricle weighed 143 g., the left ventricle 148 g. This gives a left to right ratio of 0·96 against the normal 1·79 (Lewis, 1914). The heart was greatly enlarged by dilatation of all its chambers, particularly those on the right.

The right ventricle showed great hypertrophy of the myocardium which measured 11 mm. half-way to the apex. The tricuspid ring was dilated (15 cm. circumference) and so was the pulmonary ring (9 cm.). The mitral ring was much dilated (12 cm.) but the aortic ring (6·5 cm.) was normal. The endocardium was normal throughout, as were all the valves and there were no developmental abnormalities. The pulmonary artery was uniformly distended and showed patches of atheroma and mural thrombosis. Its main and medium-sized branches were dilated but normal. The aorta appeared to be smaller than normal, both compared with the pulmonary artery and with the general body build.

Respiratory system. The larynx was normal but the left vocal cord was nearer the mid-line than the right. Both pleural cavities were obliterated by old pale fibrous adhesions. The lungs were pale and œdematous but there was no evidence of inflammatory disease or infarction. The tracheo-bronchial lymph-glands were normal.

Abdominal viscera. The peritoneal cavity contained 200 ml. of clear yellow fluid. The liver (2045 g.) was moderately enlarged with changes typical of passive congestion.

Microscopical. The right ventricle showed hypertrophy of the myocardial cells. The left ventricle was normal. Interest was centred on the pulmonary vasculature.

Sections from the hilum of each lung showed atheroma and mural thrombosis of the main branches of the pulmonary artery, which diminished peripherally till in vessels of about 3 mm. diameter it was no longer seen. The smaller vessels were dilated but otherwise normal. A section from the periphery of the lung showed what appeared to be two small bronchial arteries, the lumen of which was obliterated by intimal thickening (see Fig. 3).

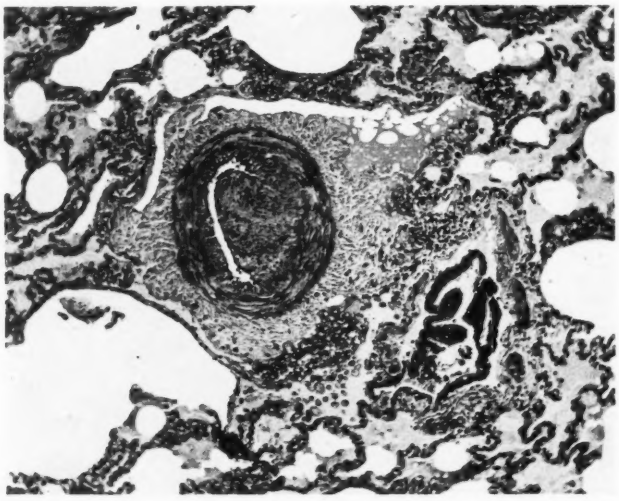


FIG. 3.—Photomicrograph from the periphery of the right lung, showing a medium-sized artery, the lumen of which is greatly narrowed by what appears to be an organized thrombus. H and E. Magnification, ×75.

A section of the right lung taken from the hilum showed two separate conglomerations of entangled blood-vessels which consisted of arteries and veins communicating with each other, forming complicated arteriovenous aneurysms (Fig. 4 and 5). Both these aneurysms lay close to large bronchi. Serial sections of the entire block made to follow the course of these aneurysms showed that they eventually resolved into a large artery and a large vein with an intercommunicating lumen. Although it was impossible to identify the anatomy of these blood vessels with certainty,

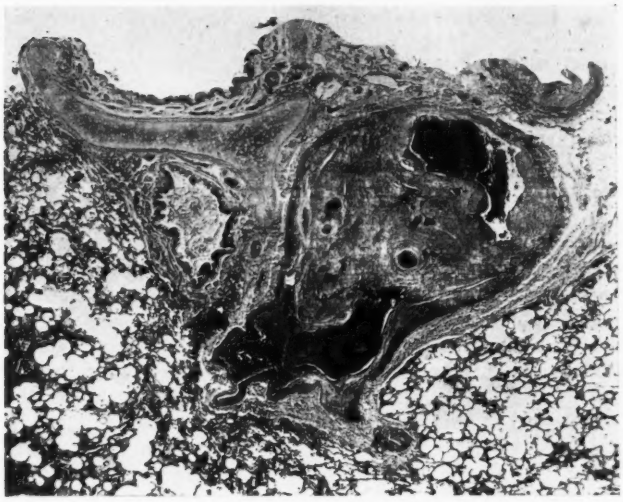


FIG. 4.—Photomicrograph of hilum of right lung, showing mass of intercommunicating blood-vessels by the side of a bronchus. H and E. Magnification, ×12.

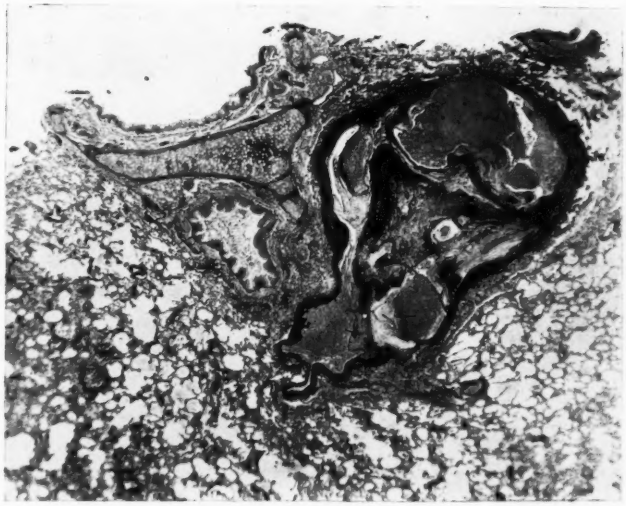


FIG. 5.—Photomicrograph from the same block stained by Weigert's elastic stain, showing abundant elastic tissue in the walls of the communicating vessels. Weigert's stain. Magnification, ×12.

the morphology of the walls with their relative difference in the elastic and muscular components, suggested that the malformations were between bronchial arteries and pulmonary arteries and veins.

Sections from the lung showed moderate passive congestion with œdema and heart-failure cells in the alveoli. Another section from the periphery showed moderate emphysema and focal œdema. There was no evidence of inflammatory disease or of infarction.

X

Discussion

Can this case be accepted as one of primary pulmonary hypertension? It is suggested that the term is justified by the isolated right ventricular hypertrophy, with dilatation and early sclerosis of the pulmonary artery without adequate pulmonary disease. Must the arteriovenous aneurysm found at the right hilum be regarded as causally related to the patient's illness? Here it must be admitted that the existence of so unusual an abnormality of the lung, in a patient who has died of a rare disease of the pulmonary vasculature of unknown ætiology, justifies this assumption as a working hypothesis.

Before death the diagnosis of auricular septal defect was made with some confidence, from the signs of increased blood flow and pressure in the pulmonary artery. At the autopsy it appeared that all the circumstances were present, from which the diagnosis of this anomaly is usually made, except for the septal defect itself. East (1940) in describing his case of primary pulmonary hypertension, makes it clear that the same signs had made the same diagnosis plausible. It was therefore natural to consider what circumstances could have a similar effect upon the dynamics of the lesser circulation. The only comparable situation, in which blood from the right ventricle might pass through a peripheral channel to return to the right auricle and thus round again, would be if there were a communication between the pulmonary artery and a bronchial vein. This was purely hypothetical, but it was to investigate this possibility that sections from the hila were specially asked for, and in one of these the arteriovenous communication was found. The presence of a systemic artery, shown by serial sections to be contributing to the aneurysm, makes it necessary to abandon the original hypothesis. The only alternative is an anastomosis between bronchial artery and pulmonary artery or vein.

In the developing lung the early pulmonary capillary plexus is fed by ventral branches of the dorsal aorta and this is its only source of supply until the pulmonary artery develops later from the ventral root of the sixth branchial arch. When the pulmonary artery takes over, the aortic connections regress until at birth they are represented by the bronchial arteries only. This process is well described by Huntington (1919), who states " the origin and variations of the bronchial arteries and the presence of anastomoses or larger connecting channels between them and the pulmonary arteries, depends on the organization of the early postbranchial pulmonary plexus."

When the bronchial arteries were rediscovered by Ruysch in 1732, he assumed that they anastomosed with the pulmonary artery and this belief was maintained until fairly recent times. But it is now generally accepted that there is no direct arterial anastomosis in normal health. The experiments of W. S. Miller (1892–1925) using injection methods and of Berry and Daly (1931) using the heart-lung preparation, agree in demonstrating that the two arterial systems communicate only through the capillary bed to which both contribute. These experiments were done on the lungs of dogs in normal health. On the other hand, Rakshit (1949) has recently demonstrated vessels that connect the bronchial with the pulmonary artery in the lung hila of the guinea-pig and the rat.

It has long been known that in cases of congenital pulmonary atresia there is hypertrophy of the bronchial arteries with direct communications between them and the pulmonary arteries. Wood and M. Miller (1938) in an important paper describing the result of injections of dye into the aorta when all exits from the aorta were ligatured except the bronchial arteries, were able to demonstrate greatly increased communications between the bronchial and pulmonary arteries in certain diseases. These abnormal communications occurred generally in cases of mitral stenosis and locally in cases of primary bronchial carcinoma and in pulmonary tuberculosis. In the latter disease, when the subject had died after a hæmoptysis, the injection mass derived from the aorta was found in the cavity, suggesting that the fatal hæmorrhage had occurred from the bronchial artery. Most significantly to this paper, one of their 74 patients, diagnosed " Ayerza's disease " but from the description evidently an example of primary pulmonary hypertension, showed on injection of the aorta a complete outline of the pulmonary arterial tree. The vascular shunt between the two circulations was in this case greater than in any other and although no histological examination

is mentioned, the underlying abnormality must have been something very like that found in the present case.

Cauldwell *et al.* (1948) confirm these observations as regards pulmonary tuberculosis, but there are few other reports as to the possibility of such shunts. Hovelacque *et al.* (1936) in an anatomical investigation of the bronchial arterial system, found in 6 of the 30 subjects they examined a direct extrapulmonary anastomosis between a main bronchial artery and a pulmonary vein. They illustrate one of these and certainly the contributing bronchial artery appears to be more than a mere vas vasorum: there is no note as to the cause of death in their cases. There is, too, no confirmation of this finding in the much more extensive work on the same subject by Cauldwell *et al.* (1948).

Taussig (1947) describes a case of Eisenmenger's complex in which " the pulmonary artery was enormously enlarged and there were remarkable changes in the lungs which resembled arteriovenous aneurysms." It is not likely that these were pulmonary arteriovenous communications of the usual sort for the patient was not cyanosed until the age of 16. Elsewhere, Taussig stresses the difficulty of distinguishing clinically between the Eisenmenger complex and " Ayerza's disease."

It is here suggested that primary pulmonary hypertension results from the excessive entry of blood into the lesser circulation from the bronchial arteries. This blood, being injected under systemic pressure causes dilatation and sclerotic changes in the pulmonary artery and hypertrophy with eventual failure of the right ventricle. In the case under review the abnormal communication may have been a developmental abnormality, a failure of regression of the ventral branches of the dorsal aorta within the lung. Such an anastomosis, established potentially before birth, would tend in the course of years to carry increasing quantities of blood, and thus eventually to cause death from right ventricular failure.

It should be possible in future cases to test this hypothesis by post-mortem injection methods such as those of Wood and Miller (1938), followed by a search of the hila for anastomoses. If it be allowed that these anastomoses may occur spontaneously, then a method of treatment by ligation of the bronchial arteries may arise, in those cases that are not too far advanced to preclude a thoracotomy.

Summary

A case of primary pulmonary hypertension is presented which showed paralysis of the left vocal cord.

At necropsy an arteriovenous communication was found; this was probably an anastomosis between bronchial artery and pulmonary artery.

The significance of this finding is discussed.

My thanks are due to Dr. W. N. Mann under whom the patient was admitted to Guy's Hospital, to Dr. S. J. De Navasquez for his help in the histology, and to Dr. Maurice Campbell for his general advice. I am also grateful to Brigadier Bennett, Consultant Physician to the Army, for permitting me to see the patient's previous case-notes.

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ABSTRACTS OF CARDIOLOGY

Angiocardiographic Study of the Pulmonary Artery. C. T. DOTTER and I. STEINBERG. *J. Amer. med. Ass.* **139**, 566–572, Feb. 26, 1949.

Congenital and acquired heart disease, as well as pulmonary disease produce significant changes in the size and configuration of the pulmonary artery and its branches which can best be studied by means of angiocardiography. Dilatation of the pulmonary artery can be demonstrated in cases of congenital aneurysm and septal defect, being particularly marked in Lutembacher's syndrome. In cases of patent ductus arteriosus the widening is well demonstrated, as also is the retrograde flow coincident with aortic filling. Angiocardiography is of particular value in differentiating Eisenmenger's syndrome from the tetralogy of Fallot. In the former, the dilated pulmonary artery is visible; in the latter, if visualized at all, it is small. In cases of pulmonary stenosis the exact location of the narrowing may be demonstrated, the artery distal to the obstruction being found on occasion to be dilated.

In cases of acquired disease of the aortic valve no significant changes are demonstrated in the pulmonary artery in the absence of cardiac failure. In acquired mitral disease elongation of the outflow tract is seen, sometimes associated with dilatation of the pulmonary trunk. Syphilitic aneurysms can also be well demonstrated. It is suggested that the diagnosis of cor pulmonale can be made far in advance of the appearance of cyanosis by the angiocardiographic demonstration of elongation of the pulmonary outflow tract followed by moderate dilatation of the bed of the pulmonary trunk.

L. G. Blair

The Electrocardiographic Effects of Smoking Tobacco. III. Patients with Coronary Disease. B. VON AHN. *Nord. Med.*, **41**, 451–456, March 11, 1949.

Thirty patients suffering from coronary disease, of whom 20 had angina pectoris (said in 4 cases to be brought on by smoking), were subjected to an examination designed to elucidate the effect of smoking on the coronary vessels. After 30 minutes' rest, an electrocardiogram was taken and the patients then chain-smoked until toxic symptoms appeared (an average of 45 minutes). The electrocardiogram was recorded at 3-minute intervals throughout the test. There was an average rise in systolic and diastolic blood pressures of 12 mm. Hg and a rise in pulse rate of 11 beats a minute. In only one case was there an appreciable change in the electrocardiogram; this patient was a 64-year-old non-smoker with bundle-branch block and extrasystoles, and the effect of smoking was to increase very considerably the frequency of the extrasystoles. In 2 patients anginal attacks developed when the blood pressure was at its height. In 9 cases, no change was observed in the electrocardiogram recorded during exercise both before and after smoking. The author concludes that any deleterious effect of smoking on the heart must be a secondary effect of the rise in blood pressure (especially in diastolic pressure) that occurs, rather than a direct action on the coronary vessels. Smoking should therefore be forbidden in cases where it induces a marked rise in the diastolic pressure (20 mm. Hg or more). He is of the opinion that tobacco angina, though it undoubtedly exists, is a very rare phenomenon.

B. Nordin

Diagnostic Use of Tetræthylammonium Chloride (Etamon) in Occlusive Arterial Disease of the Extremities. J. FARR and J. DOUPE. *Canad. J. Res.* (*E*) **27**, 4–9, Feb., 1949.

Tetræthylammonium chloride ("etamon") paralyses autonomic ganglia and produces hypotension and peripheral vasodilatation. The effects of the intravenous injection of "etamon" in doses of 300 to 500 mg. were compared with reflex thermal vasodilatation in 14 subjects, of whom 3 were normal and 11 had peripheral vascular disease. In no case did "etamon" produce the higher digital skin temperature, and the mean maximum skin temperature after "etamon" was 5° to 6° C. lower than after body heating. The authors conclude that "etamon" is not a reliable agent for testing the power of dilatation of the peripheral circulation.

A. S. Dixon

Angiocardiography in Congenital Heart Disease. (Technique and Results in 74 Cases.) E. DONZELOT, A. M. EMAM-ZADE, R. HEIM DE BALSAC, J. E. ESCALLE, and M. ANTOINE. *Arch. Mal. Cœur*, **42**, 35–49, Jan., 1949. 6 figs., 26 refs.

Angiocardiography with 70% "diodrast" was attempted in 74 patients with congenital heart disease. These patients were selected from a much larger group, because in them the investigation might have been expected to provide a more exact diagnosis or to demonstrate the course of a particular blood vessel. Without local analgesia or exposure of the vein, a trocar either 17/10 or 25/10 in size was pushed into the external jugular vein (this vein was chosen as being accessible and giving direct access to the heart and great vessels) and 15 to 70 ml. of diodrast in a dosage of 1 ml. per kg. of body weight was injected.

Five illustrative cases submitted to the investigation

are discussed. The authors regard angiocardiography as a laborious method, not dangerous, and of decided value in the pre-operative investigation of congenital heart disease. *H. E. Holling*

Study of 200 Cases of Tetralogy of Fallot. E. DONZELOT, R. H. DE BALSAC, A. M. EMAM-ZADE, J. E. ESCALLE, and C. METIANU. *Arch. Mal. Cœur*, **42**, 98–137, 1949.

The Eisenmenger Complex. Study of 29 Cases. E. DONZELOT, A. M. EMAM-ZADE, R. H. DE BALSAC, and M. KOLOSY. *Arch. Mal. Cœur*, **42**, 138–166, 1949.

Study of the Volumetric Increase in the Pulmonary Artery in a Series of 314 Cases of Congenital Heart Disease. E. DONZELOT, A. M., EMAM-ZADE, R. H. DE BALZAC, J. E. ESCALLE, and C. METIANU. *Arch. Mal. Cœur*, **42**, 167–195, 1949.

The authors report in three articles the results of a year's work at the " blue baby " centre of the Broussais Hospital. The first deals with 200 cases of Fallot's tetralogy. Operative results are analysed and the diagnosis and treatment discussed. The second describes 29 cases of Eisenmenger's complex, and points out that angiocardiography is the most important diagnostic procedure in such cases. The third article groups all cases with dilatation, in whole or in part, of the pulmonary artery or its branches. The authors conclude that, where the pulmonary artery arises from the centre of the base of the heart, angiocardiography furnishes the sole evidence of its enlargement. *A. S. Dixon*

A Comparison of Precordial Electrocardiograms Obtained with CR, CL, CF, and V leads. M. DOLGIN, S. GRAU, and L. N. KATZ. *Amer. Heart J.*, **37**, 343–358, March, 1949.

The purpose of this study was to compare the CR, CL CF. and V leads recorded in identical præcordial positions in health and in certain abnormal states: posterior-wall infarction, emphysema, and non-specific electrocardiographic abnormalities. Examples of four types of electrocardiogram are presented to show that the difference between these leads may be great enough to affect the interpretation. In most cases, however, it probably makes little difference whether the indifferent electrode is placed on the right arm, left arm, left leg, or is attached to the central terminal. *A. Brown*

VII. Correlation of Electrocardiographic and Pathologic Findings in Lateral Infarction. G. B. MYERS, H. A. KLEIN, and B. E. STOFER. *Amer. Heart J.*, **37**, 374–417, March, 1949. 20 figs., 17 refs.

In 14 of 27 cases of lateral infarction verified at necropsy the infarct was mainly basal (high lateral infarct). In these the findings with præcordial leads were seldom distinctive, and changes might be limited to V3 and V4. Lead aVL was abnormal in 11 cases.

In 11 cases the apical third of the lateral wall was infarcted. In 8 changes were found in V5 and V6, as well as in lead aVL, which were strongly suggestive or diagnostic of infarction. In 2 a marked depression of the R–ST junction was found in leads V4 and V5 as described by Wolferth and Wood. In these cases the infarct affected principally the middle portion of the wall, the sub-epicardial zone being spared. In 2 cases the infarct involved the middle third of the lateral wall. Both infarcts were small and sub-endocardial. The electrocardiographical changes were those described by Wolferth and Wood.

It is concluded that in order to diagnose a lateral infarct that is not mainly apical it is necessary to employ additional præcordial leads in the 3rd intercostal space. *C. W. C. Bain*

The Control of Arrhythmias occurring during Operation upon the Valves of the Heart: Experimental and Clinical Observations. H. G. SMITHY. *Sth. Surg.* **14**, 611–618, Sept., 1948.

Irregularities in heart action are commonly noted whenever the heart is handled at operation; and it is a matter of even greater significance where the damaged human heart has to be considered. The common irregularities are ventricular extrasystoles, tachycardia, fibrillation, and complete disorganization.

The author carried out experiments on animals in which he applied procaine locally to the surface, infiltrated the heart muscle with 2% procaine, injected the same drug both intravenously and directly into the interventricular septum and gave intravenous injections of quinidine. The direct injection of procaine into the myocardium and intravenous injection of quinidine were the only methods that had any practical application.

The author has operated on 8 patients with mitral stenosis. Pre-operative quinidine was given. When the pericardium was opened 5 to 20 ml. of 2% procaine was poured over the heart, and the site selected for introducing the valvulotome was infiltrated with 5 to 15 ml. of 1% procaine. In some of the patients auricular fibrillation was present before operation, and it was noted that local stimulation of the heart produced irregularities until the procaine solution had infiltrated the muscle. The author had the impression that this reduction of excessive stimulation was of great value. Of the 8 patients 2 died after operation. *T. Holmes Sellors*

Cardiocirculatory Disturbances during Intrathoracic Surgery. C. L. BURSTEIN, T. L. PIAZZA, L. A. KAPP, and E. A. ROVENSTINE. *Surgery*, **25**, 36–46, Jan., 1949.

The development of chest surgery has led to the recognition of numerous reflex reactions to intrathoracic manipulation. Efforts have been made to reduce the incidence of these by the intravenous injection of procaine, which abolishes certain arrhythmias, and by vagal block. The authors describe the reflex disturbances observed during a variety of intrathoracic operations, as

demonstrated by blood pressure and electrocardiographic records.

Manipulation of the pericardium caused marked changes of cardiac rhythm—particularly from ventricular premature beats, often of multifocal origin—and incision of the pleura also produced a variety of rhythm disturbances. Interference with the vagus nerve at the hilum of the lung resulted in bradycardia in some cases, and dissection of the vagus was accompanied in one case by a profound fall in blood pressure followed by a rise to well above the initial level. These reactions occurred in spite of procaine injections into the vagus and into the pulmonary plexus. Rib scraping and intercostal-nerve stimulation also induced reflex rhythm changes. The effects of changes of position were also of great importance; turning a patient on to the healthy side, even before the pleura was opened, resulted in a fall in blood pressure from 140 to 80 mm. Hg. Such procedures were even more deleterious when combined with the application of a chest elevator, which adds to the mechanical constriction of the chest contents, so that a " tamponade " effect may be produced.

The authors recommend that patients should be placed in the correct operative position from the outset, anæsthesia and other preliminary procedures being carried out with the patient in that position. Local infiltration of sensitive areas with procaine is also recommended.

J. McMichael

The Cardiac Mechanism During Anesthesia and Operation in Patients with Congenital Heart Disease and Cyanosis. R. F. ZIEGLER. *Bull. Johns Hopk. Hosp.*, **83**, 237–274, Sept., 1948. 9 figs., 35 refs.

Electrocardiographic studies were made on 175 children with congenital heart disease of the cyanotic type during performance of the Blalock–Taussig operation. By this method arrhythmias were detected in approximately 80% of the cases, whereas clinical methods demonstrated cardiac abnormalities only in 6%. Relatively few of these arrhythmias are of clinical significance. The main anæsthetic agents were cyclopropane and ether. Morphine premedication tended to exaggerate the arrhythmias, but atropine had an opposite effect. The cardiac abnormalities that signify impending danger are discussed. Sinus tachycardia is not significant. By contrast, marked sinus or A–V nodal bradycardia is a herald of impending cardiac asystole. This bradycardia is associated with a rate below 50 and does not respond to the administration of atropine. Other abnormal manifestations of prognostic significance are complete A–V dissociation with idioventricular rhythm, ventricular tachycardia, complete bundle-branch block, important S–T deviation, and sinus arrest. Complete heart block and sinus arrest occurred only terminally and thus not early enough for prophylactic or therapeutic steps to be taken.

The most important factor that contributes to cardiac standstill is anoxæmia. Other important factors included vagal stimulation, action of the anæsthetic agent on the myocardium, decreased cardiac output with positive endotracheal pressure, adrenal-cortical insufficiency, and potassium inhibition.

If frequent ventricular premature systoles occur at operation cyclopropane should be stopped and anæsthesia continued with ether and oxygen. In ectopic tachycardias the vagus is best stimulated by the intravenous injection of the purified glycoside of digitalis. Atropine should not be given as premedication to patients with a history of paroxysmal tachycardia. In bradycardia atropine produces a reversion to normal sinus rhythm or sinus tachycardia. If there be no response to atropine, a rate below 50 is a danger signal before the onset of terminal cardiac asystole. Steps to combat the underlying anoxæmia include periodic inflation of the collapsed lung; it is important to combat the co-existing anæmia and to give cardiac stimulants, such as adrenaline. If cardiac dilatation and arrest occur cardiac massage and artificial respiration with a high concentration of oxygen should be undertaken at once. Intracardiac adrenalin is of questionable value, although ventricular fibrillation has not been observed among the patients studied in this series. The author seems to prefer the use of digitalis in maintaining normal cardiac contractions during anæsthesia and operation.

A. I. Suchett-Kaye

Traitement Chirurgical de l'Hypertension Arterielle. MAURICE LUZUY and JEAN F. PORGE. Published by G. Doin and Co. of Paris. 160 pp., 58 fis. 500 fr.

This volume is composed mainly of the observations of one of the authors (M. L.) on the various forms of treatment of essential hypertension which he saw carried out in the United States. It is written in collaboration with a physician (J. P.) and gives a concise survey of the present knowledge on hypertension, and also goes into the physiopathological justification of surgical treatment.

The book is most useful for anybody interested in the treatment of hypertension, particularly surgeons contemplating operative attack on the disease. All the better-known methods are clearly described, and good illustrations make the various techniques easy to follow. Short chapters on renal and adrenal hypertension are included, and an assessment is made of the choice of the various surgical methods.

Frank D'Abreu

Technique de la Chirurgie du Sympathique et de ses Infiltrations. O. LAMBRET, P. RAZEMON, and P. DECOULX. Third Edition. Published by G. Doin and Co., Paris. 240 pp., 106 illus., 4 pls.

This book—a product of the Faculty of Medicine at Lille—has proved its popularity by the necessity for a third edition. The technique of operations upon the sympathetic nerve system, including infiltrations of the cervical ganglion, carotid sinus, the splanchnic, lumbar and hypogastric sympathetic systems, including surgical ablations of various portions of the sympathetic system are shortly and clearly described. Illustrations demonstrating the techniques of infiltrations and of operations are unusually clear and helpful.

The sections on lumbodorsal sympathectomy and on the surgical treatment of hypertension could well be enlarged, only the original Smithwick technique being described at any length.

The volume forms a useful book of reference for those taking up the surgery of the sympathetic nerve system.

Frank D'Abreu

La Vectocardiographie. P. W. DUCHOSAL and R. SULZER. S. Karger, Basle, 1949. 172 pp. with 88 figs.

The authors of this monograph have integrated in one sequence of argument, mathematical analysis, technique and interpretation, the work carried on by them in this field during more than a decade and published in a series of papers in various journals. Many of their articles appeared during the war years in Swiss journals.

The sum of all the electromotive forces in the heart at any instant can be regarded as a vector of given magnitude and orientation in three-dimensional space. During the cardiac cycle the vector varies in magnitude and orientation continually from one instant to the next. In the conventional standard three leads, one is recording the projection on each lead in turn of the component of the vector in the frontal plane, as is familiar from the classical Einthoven triangle figure. In vectorcardiography the aim is to record the orientation in space and the magnitude of the vector continuously throughout the cardiac cycle.

Using three-dimensional points of application for the electrodes, the action currents are led through amplifiers to a " split-beam " cathode-ray tube, permitting the simultaneous recording of leads in two planes at right angles to one another. The wanderings of the luminous spots on the two screens during a single cardiac cycle are recorded photographically. The path traced is always a loop, the form of which varies greatly in healthy and diseased hearts. By recording leads in these planes (horizontal, sagittal and frontal) the authors have succeeded by a laborious if ingenious method in reconstructing in pliable wire a three-dimensional model of the vector path—a " stereo-vectogram."

The technical difficulties of the procedure are formidable. The electrical and photographic apparatus is complicated; the electrodes are not applied at random to the trunk, but to points selected after careful measurement from the cardiac centre; the patient must lie during the recording in a screened cage to avoid electrical interference. The authors estimate the time necessary for a recording as one hour, plus 1½ hours for enlargement and analysis of the vectograms. These technical considerations thus render this a method for research rather than for routine clinical work.

The unique properties of the vectocardiogram become apparent in the section of the monograph devoted to analysis and comparison with other leads. By analysis one can extract the curve of any desired electrocardiographic lead—standard, unipolar limb, or even unipolar præcordial. The numerous examples figured show a very close correspondence.

There is a full discussion of the physical basis for this property, which is at once a confirmation of Wilson's views on the nature of potential distribution in the body regarded as a conductor, and a refutation of current ideas on the nature of præcordial or " semi-direct " leads.

Clearly written, well illustrated and printed, and with a full bibliography, the book is recommended for study by all interested in the basic problems of electrocardiography.

I. G. W. Hill

Measurements of Heart Output by Electrokymography. G. C. RING, M. BALABAN, and M. J. OPPENHEIMER. *Amer. J. Physiol.* **157**, 343–351, June, 1949.

This is a preliminary account of a new electrokymographic method for the measurement of cardiac output. The antero-posterior thickness of the ventricles in systole and diastole is determined by measuring the amount of X-ray transmission in each phase and the heart output calculated according to a formula worked out by the authors. The advantage claimed for the new method is that subjective errors inherent in older techniques are eliminated. The results obtained in 31 subjects are compared with those obtained simultaneously by ballistocardiography.

A. I. Suchett-Kaye

The Action of Sodium Thiocyanate on Cardiac Output. Z. M. BACQ, R. CHARLIER, E. PHILIPPOT, and P. FISCHER. *Brit. J. Pharmacol.*, **4**, 162–167, 1949.

In view of the introduction of sodium thiocyanate for the treatment of hypertension in man, its effects on the heart were studied in dogs under chloralose anæsthesia. Cardiac output, as calculated from the Fick principle, was decreased by the intravenous injection of thiocyanate in 5 dogs out of 6. The heart rate was usually decreased but the arterial blood pressure did not change, indicating that vascular constriction had taken place. There was no obvious relation between dose and response. From these observations, together with others cited from the literature, it is concluded that thiocyanate exerts its action by increasing the response of the heart to vagal tone and, that this is effected through a sensitization of the heart muscle to potassium ions. Thiocyanate, therefore, weakens the heart and the authors point out the dangers of using such a drug in the treatment of hypertension. They also recommend calcium as an antidote in thiocyanate intoxication.

John R. Vane

A Study of Pericarditis in the Light of a Series Observed in Finland. I. Etiology and Pathogenesis of Exudative Pericarditis. M. SAVILAHTI. *Ann. Med. intern. fenn.*, **38**, 52–69, 1949.

In each of two series, one of 3,054 consecutive necropsies and one of 55,699 clinical reports, the author found 127 cases of serofibrinous or purulent pericarditis, the condition being discovered approximately 20 times oftener post mortem than during life. Purulent pulmonary and pleural conditions were commoner causes of the disease than were rheumatic fever and tuberculosis. In all groups, excluding the cases of

rheumatism, pericarditis was commoner in males by 3 to 2, and the average age of the patient was 30 years.

Whereas tuberculous pericarditis was usually diagnosed correctly during life, in other conditions the clinical manifestations of the primary disease often overshadowed the pericarditis; in 80% of cases its presence had been unsuspected by the clinician, yet in many instances pericarditis was the most important necropsy finding. All cases of purulent pericarditis, for example, remained undiscovered until necropsy. No satisfactory conclusions could be drawn as regards the incidence of uræmic pericarditis and pericarditis following cardiac infarction.

There was some evidence that inflammation reached the pericardium by continuity—from the myocardium in rheumatism and from the pleura in tuberculosis, and possibly in carcinoma. Pericarditis due to carcinoma was six times commoner with tumours of the lung than with growths elsewhere. One case of actinomycotic pericarditis is reported. *J. L. Lovibond*

A Clinical Study of Subacute Bacterial Infection Confined to the Right Side of the Heart or the Pulmonary Artery. P. S. BARKER. *Amer. Heart J.*, **37**, 1054–1068, June, 1949.

The histories of 5 cases of subacute bacterial infection confined to the right side of the heart and the pulmonary artery are given, with tables showing the relevant findings in 36 reported cases.

In less than 4% of patients with subacute bacterial endocarditis the infection is confined to the right side of the heart, though in patients with a patent ductus arteriosus the infection may be confined to the ductus and the pulmonary artery. The four cardinal features of infective endocarditis—evidence of a valvular or congenital heart lesion (found in 73% of cases), fever (found in 100% of cases), embolic phenomena (found in 82% of cases) and a positive blood culture (found in 62% of cases)—are also present when the condition is confined to the right side of the heart, but blood cultures are more frequently sterile, and embolic phenomena in the systemic circulation are rarer, though pulmonary emboli may occur. *H. E. Holling*

A Venous Shunt for Advanced Mitral Stenosis. E. F. BLAND and R. H. SWEET. *J. Amer. med. Ass.*, **140**, 1259–1265, Aug. 20, 1949.

The authors describe an operation directed at relieving acute pulmonary œdema in advanced mitral stenosis by deflecting blood from the pulmonary circuit, in which pressure is high, into systemic venous channels. It should be noted that in Lutembacher's syndrome the severe mitral stenosis does not lead to lung œdema or hæmopytis, since there is a shunt available in the inter-auricular defect, and the construction of an artificial inter-auricular channel has been attempted as a form of treatment and some successful results reported.

The operation devised by the authors consists in a right thoracotomy approach through which the azygos vein is dissected out and divided so that its central or cardiac end can conveniently be approximated to a pulmonary vein. The vessel selected is the branch of the inferior pulmonary vein which leads from the dorsal lobe or apex of the lower lobe. The two veins are anastomosed by means of a 4-mm. vitallium tube and when the clamps are released a back-flow from the pulmonary vessel into the azygos vein towards the superior vena cava is apparent. This operation has been performed on 5 patients, one dying shortly after operation. The remaining 4 have shown considerable improvement. *T. Holmes Sellors*

Visceral Thrombophlebitis Migrans. I. E. GERBER and M. MENDLOWITZ. *Ann. Intern. Med.*, **30**, 560–579, March, 1949.

On a basis of 6 well-reported cases and a brief survey of the literature the authors describe idiopathic migratory phlebitis affecting the visceral veins as a distinct clinical and pathological entity.

The clinical manifestations caused by involvement of the veins in the heart, liver, lungs, and other viscera lead to most baffling and elusive bedside problems. The ætiology and pathogenesis remain " completely unclear". Hence there is no specific treatment. *G. F. Walker*

The Treatment of Angina Pectoris by Stellate-ganglion Block in the Light of Electrocardiographic Findings. H. G. STÜBINGER and W. BUSSE. *Dtsch. med. Wschr.*, **74**, 546–549, April 29, 1949.

Stellate-ganglion block was carried out in 16 patients suffering from intractable anginal pain. The improvement was considerable in 13 cases, slight in 2, and transient in 1; 5 patients were known to be still free from pain 3 to 9 months later. In 4 cases the procedure produced no change in the electrocardiogram; in the remaining 12 only minor changes in the ventricular complexes occurred. *J. R. Bignall*

The Use of the Exercise Test in the Diagnosis of Coronary Insufficiency. M. GROSSMAN, W. W. WEINSTEIN, and L. N. KATZ. *Ann. intern. Med.*, **30**, 387–397, Feb., 1949.

In cases of suspected coronary insufficiency, particularly in the younger age groups, where the history and electrocardiogram are inconclusive, further diagnostic information can be obtained from the exercise test or the anoxæmia test. The former is simpler and safer, and the authors report their results with the Master 2-step test in 151 patients, 43 of whom had definite or doubtful coronary insufficiency. Positive results related to the appearance on the electrocardiogram of ST deflections in two or more leads, T-wave changes in leads I, II, CF4, and CF5, widening of QRS, frequent extrasystoles, or A-V block. The onset of chest pain and breathlessness during the test was supportive positive evidence. The electrocardiogram sometimes does not alter until after the test, therefore a further recording should always be made during this latent period of 2 to 6 minutes. A negative response to the test does not exclude coronary disease. *J. L. Lovibond*